Úvod do strukturní analýzy farmaceutických látek

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RTG difrakce

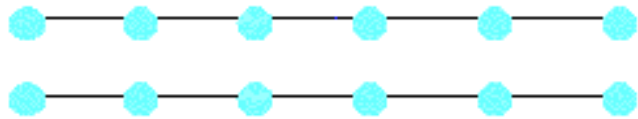
Příprava předmětu byla podpořena

projektem OPPA č. CZ.2.17/3.1.00/33253

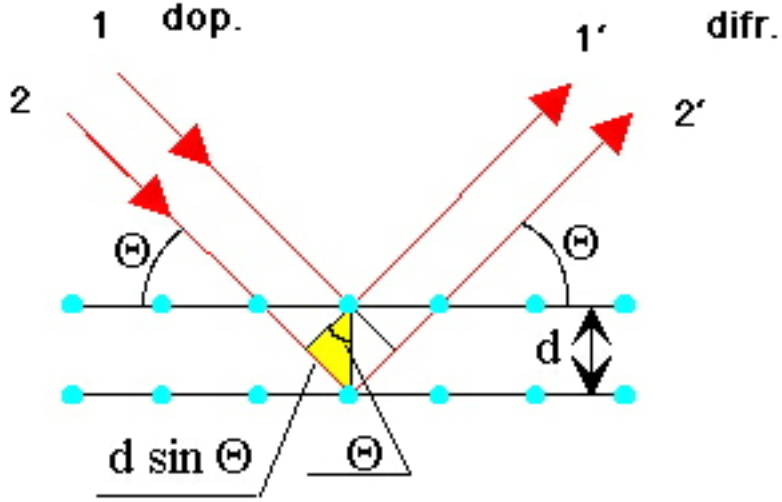
Evropský sociální fond
Praha & EU: Investujeme do vaší budoucnosti

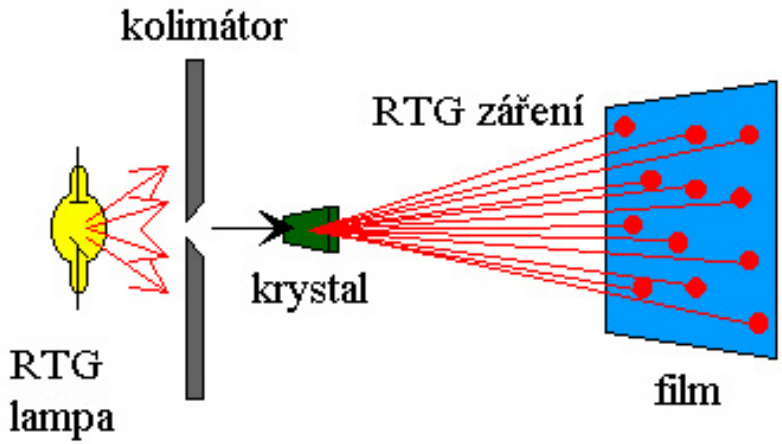
Rentgenová difraktometrie

* Princip difraktometrie –
  * ohyb (difrakce) paprsků a jejich interference

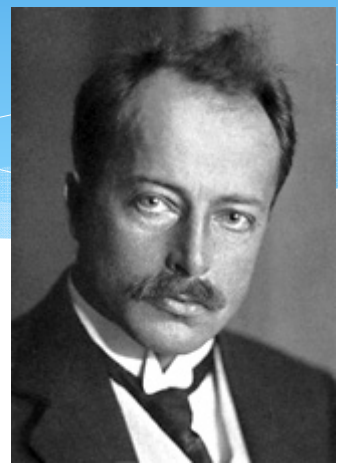


$$2d \sin \Theta = n \lambda \qquad n = 1,2,3\ldots$$





Rentgenová difraktometrie



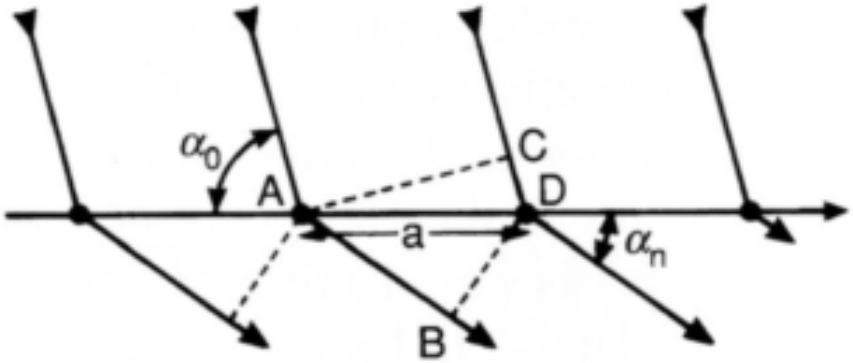
* Historické poznámky
  * Max von Laue (9. října 1879, Pfaffendorf – 24. dubna 1960, Berlín) – laueogram
  * 1912 - RTG difrakce na krystalech
  * 1914 – Nobelova cena za fyziku
  * Model difrakčního procesu – RTG záření rozkmitá elektronové obaly atomů a ty se stanou zdrojem sekundárního koherentního RTG záření, interference sekundárního záření způsobí, že v některých směrech dojde k zesílení intenzity, v jiných k zeslabení – difrakční obrazec
  * Laueovy rovnice

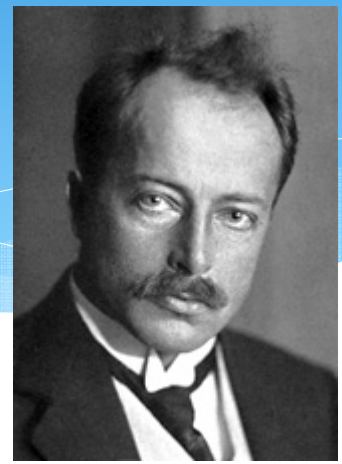
$$\boldsymbol{a}_1.(\boldsymbol{s}-\boldsymbol{s}_0)=a_1(\cos\alpha_1-\cos\alpha_{10})=k_1\lambda$$

$$\boldsymbol{a}_2.(\boldsymbol{s}-\boldsymbol{s}_0)=a_1(\cos\alpha_2-\cos\alpha_{20})=k_2\lambda$$

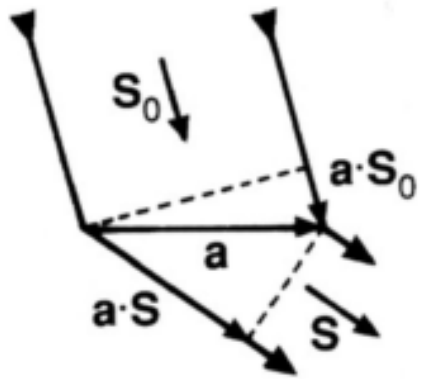
$$\boldsymbol{a}_3.(\boldsymbol{s}-\boldsymbol{s}_0)=a_3(\cos\alpha_3-\cos\alpha_{30})=k_3\lambda$$

Rentgenová difraktometrie

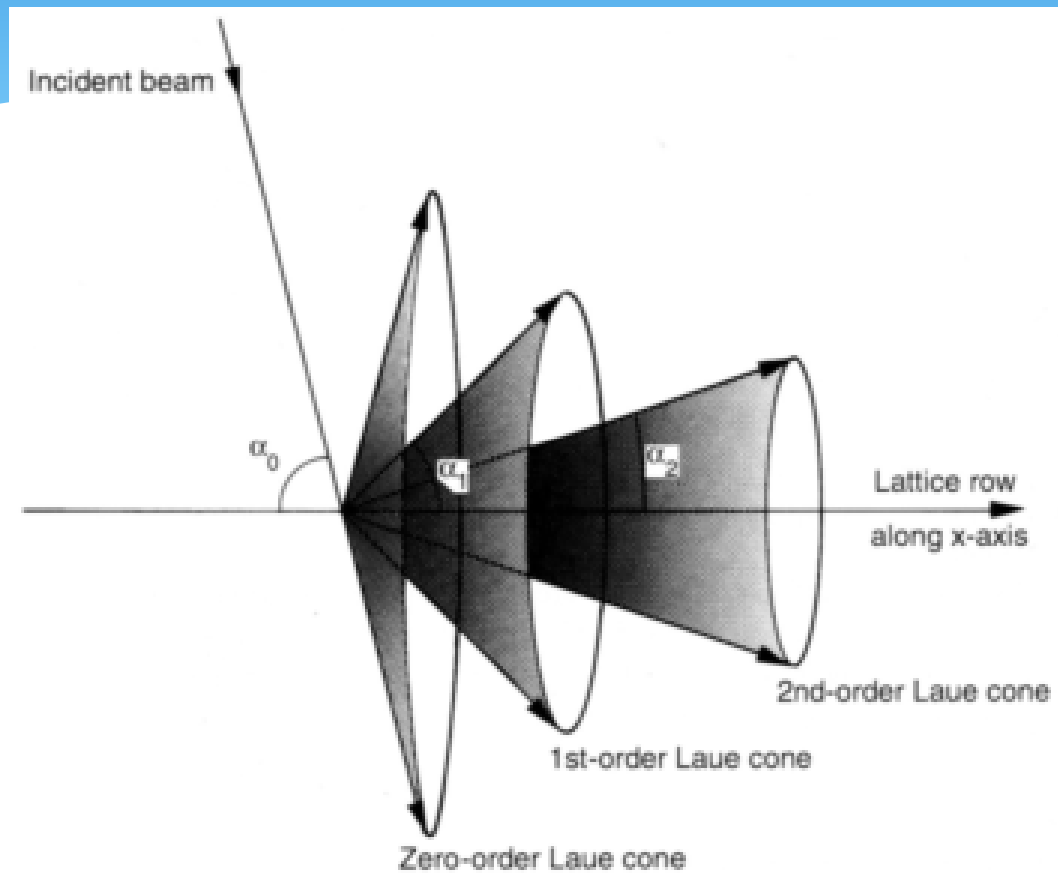


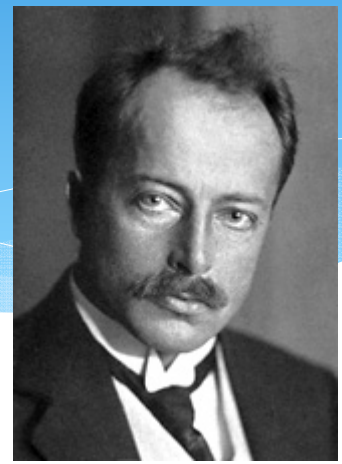


* řada atomů podél osy x s periodickou vzdáleností a
* (AB – CD) = a (cos α_n – cos α_0) = n λ
* vektorově **a** (**s** – $\mathbf{s}_0$) = a (cos α_n – cos α_0) = n λ



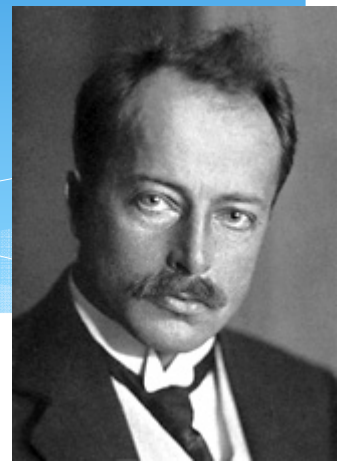
Rentgenová difraktometrie





* vektorově $\mathbf{a}\,(\mathbf{s} - \mathbf{s}_0) = a\,(\cos\alpha_n - \cos\alpha_0) = n\,\lambda$
  - podle hodnoty n (řádu difrakce) – jednotlivé (Laueho) kužely

Rentgenová difraktometrie



* vektorově **a** (**s** – **s**$_0$) = a (cos α$_n$ – cos α$_0$) = n λ

  - obdobné vyjádření pro periodicitu atomů podél další os – celkově tedy soustava rovnic

$$\boldsymbol{a}_1.(\boldsymbol{s}-\boldsymbol{s}_0)=a_1(\cos\alpha_1-\cos\alpha_{10})=k_1\lambda$$

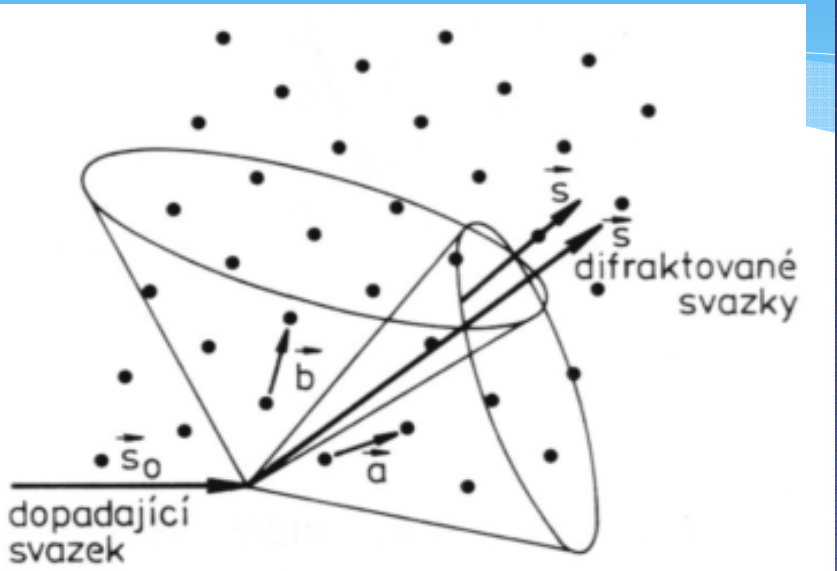
$$\boldsymbol{a}_2.(\boldsymbol{s}-\boldsymbol{s}_0)=a_1(\cos\alpha_2-\cos\alpha_{20})=k_2\lambda$$

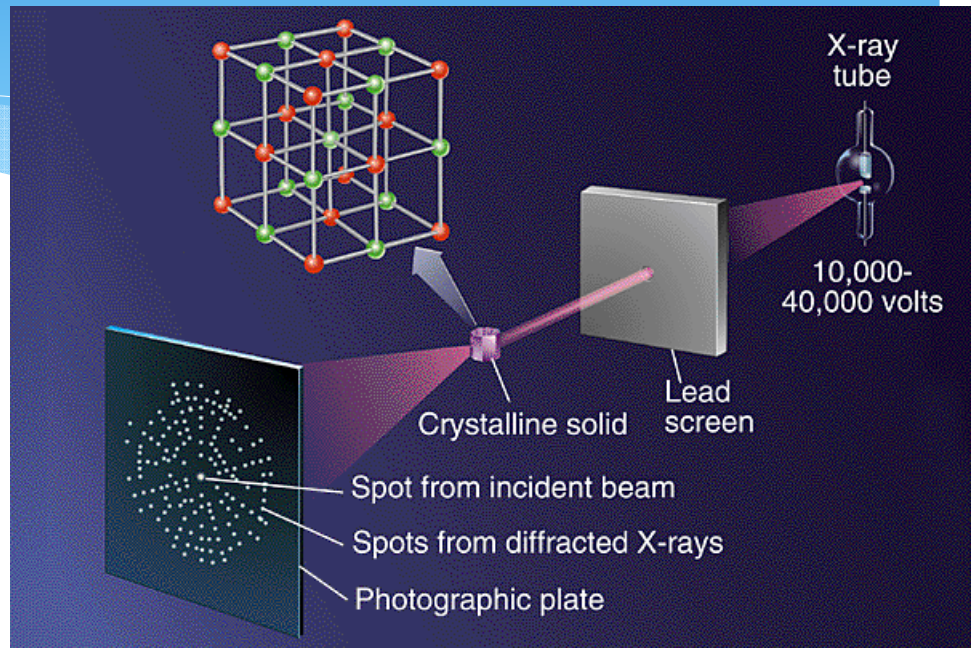
$$\boldsymbol{a}_3.(\boldsymbol{s}-\boldsymbol{s}_0)=a_3(\cos\alpha_3-\cos\alpha_{30})=k_3\lambda$$

* Parametry k_1, k_2 a k_3 značeny též h, k, l
* Nutno splnit všechny tři rovnice zároveň

Souvislost s Millerovými indexy pro kubickou symetrii

Rentgenová difraktometrie





$$\boldsymbol{a}_1.(\boldsymbol{s}-\boldsymbol{s}_0)=a_1(\cos\alpha_1-\cos\alpha_{10})=k_1\lambda$$

$$\boldsymbol{a}_2.(\boldsymbol{s}-\boldsymbol{s}_0)=a_1(\cos\alpha_2-\cos\alpha_{20})=k_2\lambda$$

$$\boldsymbol{a}_3.(\boldsymbol{s}-\boldsymbol{s}_0)=a_3(\cos\alpha_3-\cos\alpha_{30})=k_3\lambda$$

Úseky a_1, a_2 a a_3 značeny též a, b, c

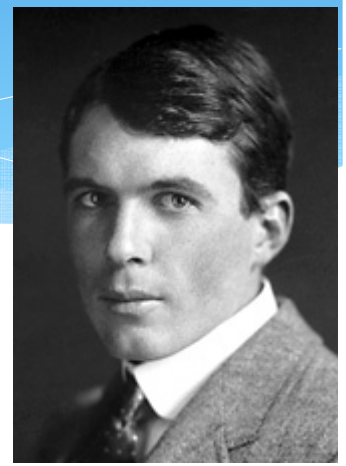
Rentgenová difraktometrie

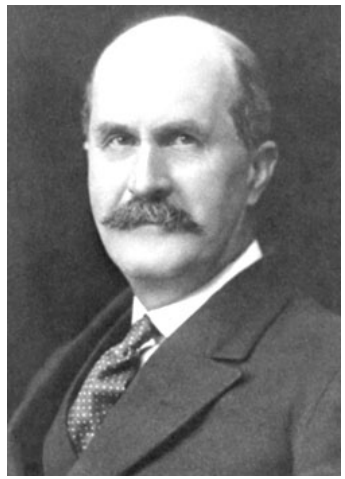
* Interakce RTG záření s elektrony atomů
* Intenzita „rozptýleného“ záření – počet elektronů v atomu (u elektroneutrálního atomu odpovídá atomovému číslu) – atomový faktor *f*
* Intenzita interferenčních maxim - populace atomů v difrakčních rovinách – Millerovy indexy
* strukturní faktor F(h,k,l) – h, k, l – Millerovy indexy
  * $u_n,\ v_n,\ w_n$ - souřadnice n-tého atomu

$$F(h,k,l,) = \sum_n f_n \exp[-2\pi i(hu_n + kv_n + lw_n),]$$

Rentgenová difraktometrie

* Historické poznámky
  * William Lawrence Bragg (31.března 1890 – 1. července 1971)
    * Matematický popis fyzikálního problému
    * Formuloval Braggovu rovnici
  * William Henry Bragg (2. července 1862 – 10. března 1942)
    * Experimentátor, konstruktér spektrometru
    * Společně Nobelova cena 1915 – analýza struktury krystalů s využitím rentgenového záření

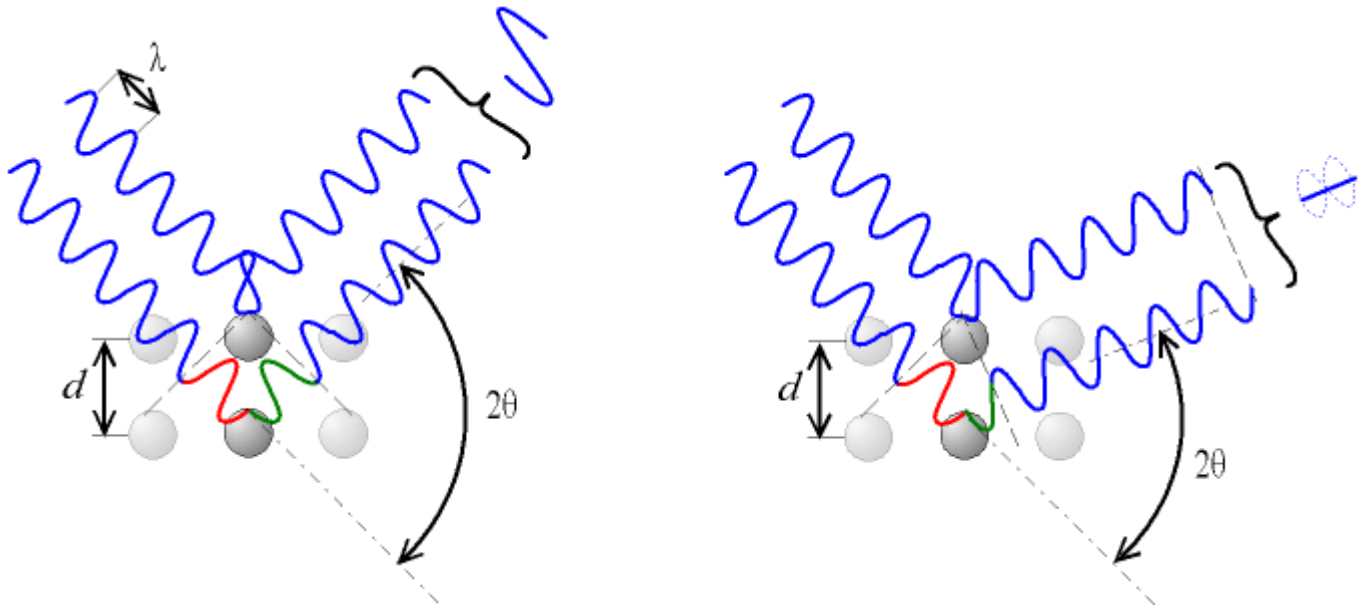




Rentgenová difraktometrie

* Braggova rovnice – interference fázově posunutých vln – model „odrazu“ na soustavě rovnoběžných krystalových rovin – fyzikálně ekvivalentní k Laueovým rovnicím

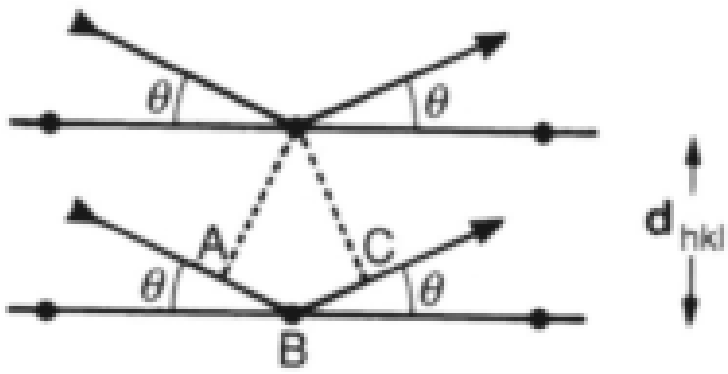
$$2d \sin \Theta = n \lambda \qquad n = 1,2,3...$$

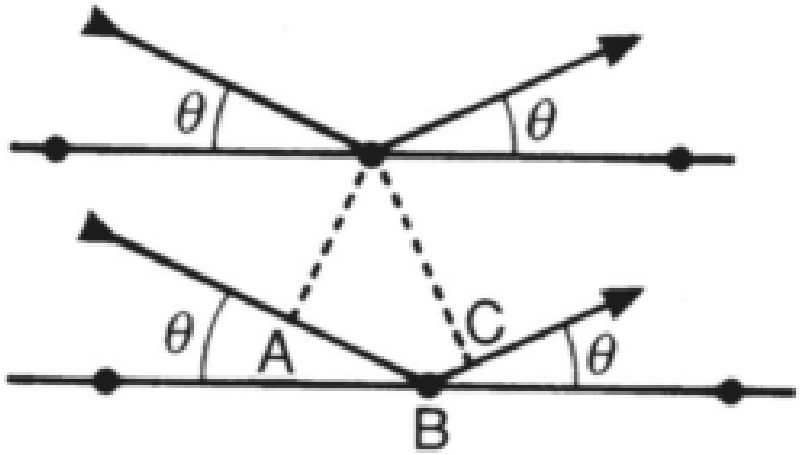


Rentgenová difraktometrie

* Braggova rovnice – aplikovatelný bez ohledu na polohy atomů v rovinách – důležitá je pouze mezirovinná vzdálenost

$$2d \sin \Theta = n \lambda \qquad n = 1,2,3...$$





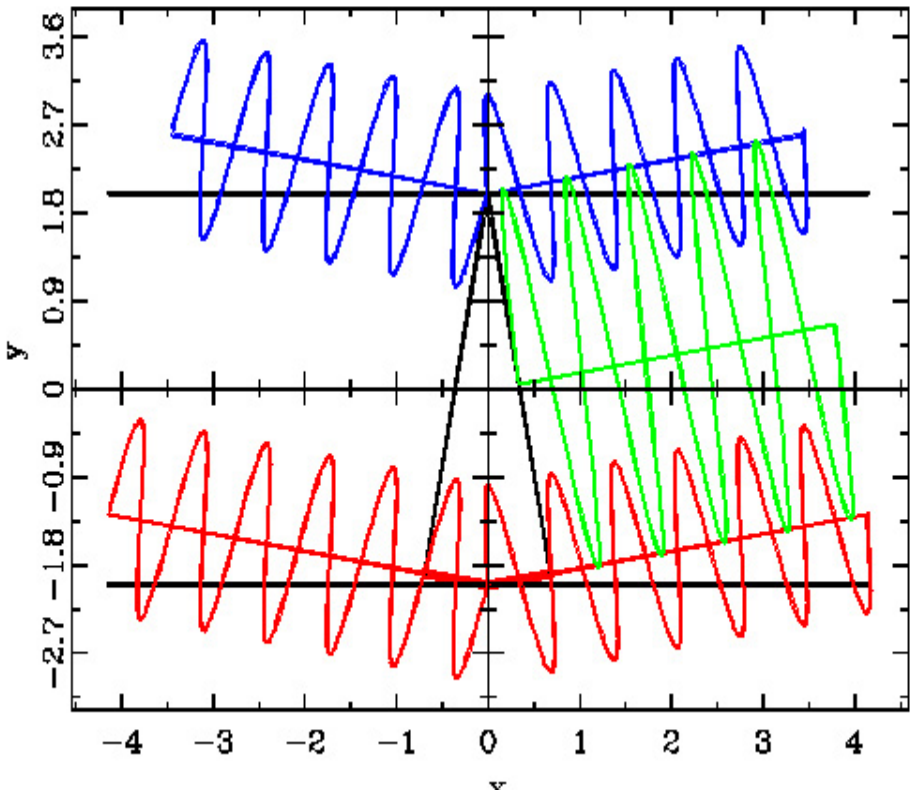
Rentgenová difraktometrie – web simulace

Bragg's law - Google Chrome

http://kr-01-032-pc1.physik.uni-erlangen.de/cgi-bin/discus/discus2.cgi?script=teach_bragg&P1=0.7&P2=&P3=0.0&P4=10&run=++RUN++&P5=0.75

Interactive Tutorial about Diffraction

Bragg's law



Wave length: 0.7

Distance between planes: 4.0

X-coordinate of atom on upper plane: 0.0

Theta: 10

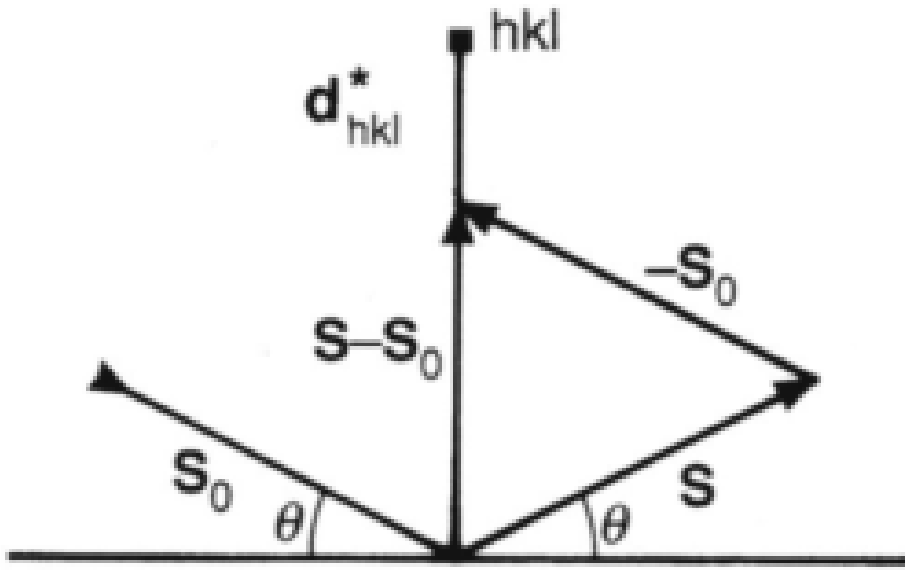
RUN

Rentgenová difraktometrie

$$2d \sin\theta = n\lambda \qquad n = 1,2,3\ldots$$

* Braggova rovnice – vektorově
* $|\mathbf{s} - \mathbf{s}_0| = 2 \sin\theta$, $d^*_{hkl} = 1/d_{hkl}$
  * $\mathbf{s} - \mathbf{s}_0 / \lambda = \mathbf{d}^*_{hkl}$

- Konstruktivní interference - když vektor $\mathbf{s} - \mathbf{s}_0 / \lambda$ souhlasí s vektorem $\mathbf{d}^*_{hkl}$

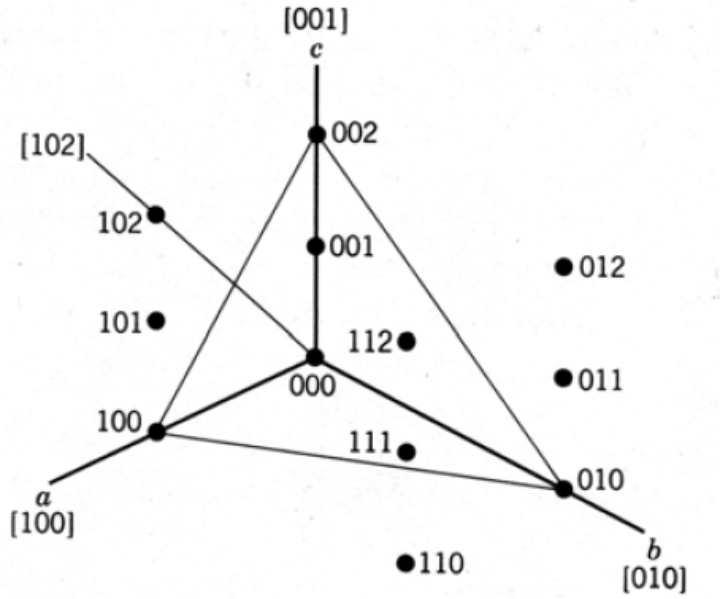


Rentgenová difraktometrie

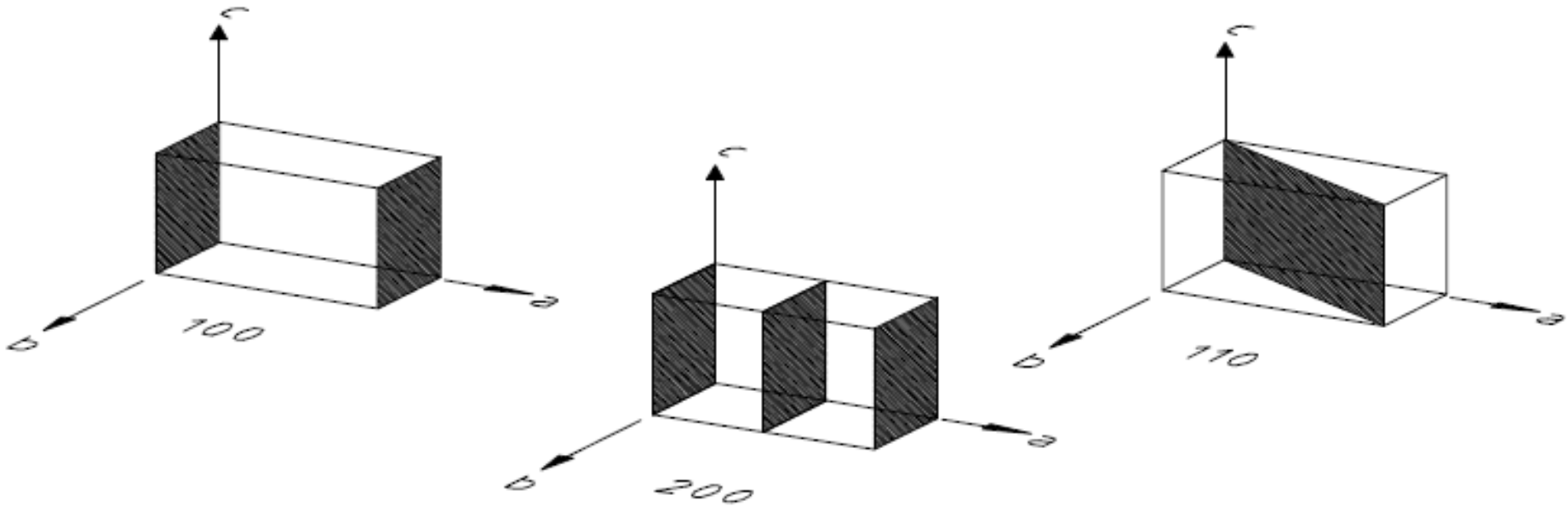
$$\sin\theta = n\lambda / 2d \quad n = 1,2,3\ldots$$

* The possible 2-THETA values where we can have reflections are determined by the unit cell dimensions.
* However, the intensities of the reflections are determined by the distribution of the electrons in the unit cell.
* The highest electron density are found around atoms. Therefore, the intensities depend on what kind of atoms we have and where in the unit cell they are located.
* Planes going through areas with high electron density will reflect strongly, planes with low electron density will give weak intensities.

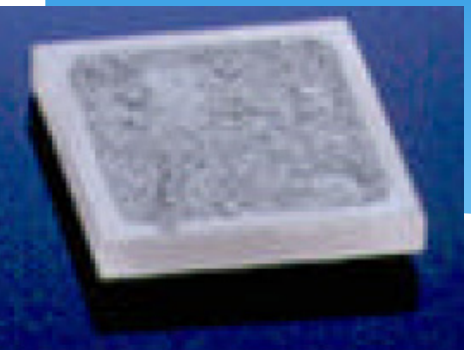
Rentgenová difraktometrie

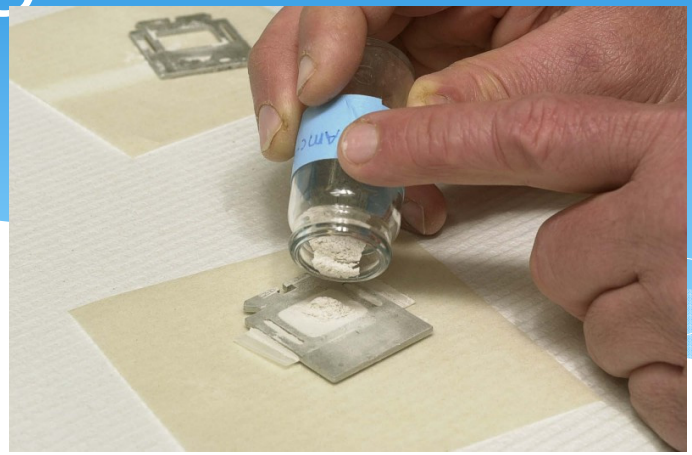


* parametry – indexy - h, k, l – čísla daná protínáním os



Rentgenová difraktometrie

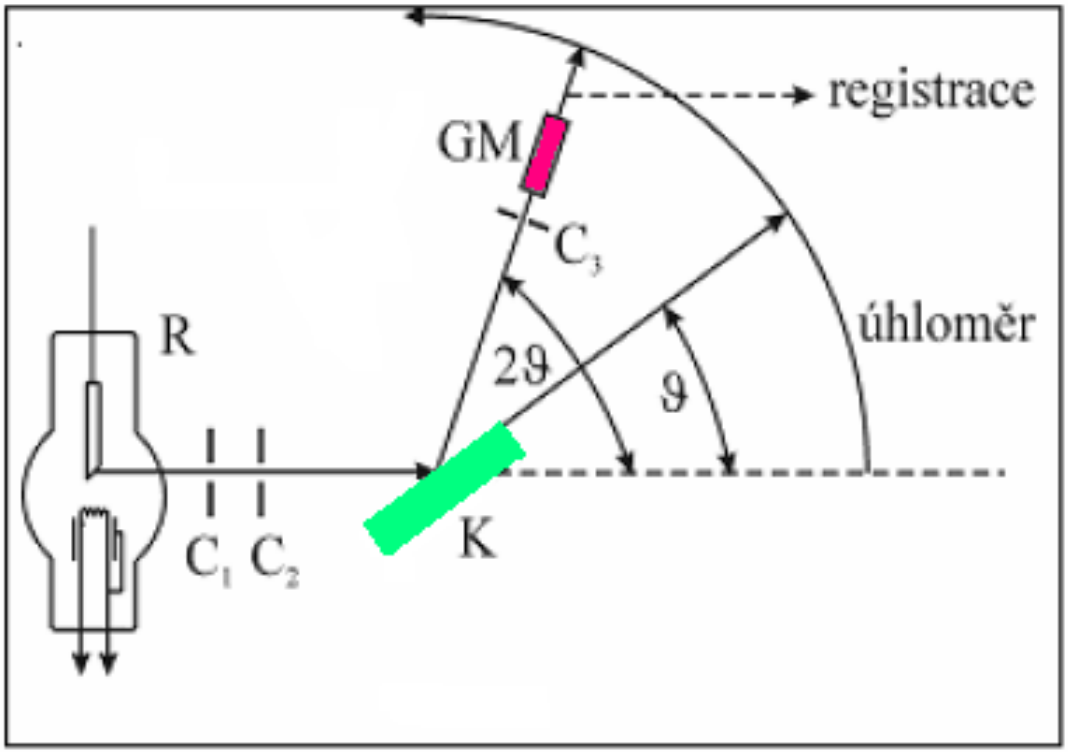




- vzorky
  - **PRÁŠKOVÉ** – polykrystalické – identifikace fází ve vzorku na principu „otisku palce“
    - Pokud možno vzorek s rovným a hladkým povrchem, rozetřený prášek – průřez částic 2 – 5 μm
    - Ideálně - homogenní vzorek s náhodnou distribucí orientace krystalitů – prášek vtlačen do držáku vzorků (běžně stovky mg)
  - **MONOKRYSTAL** – běžné požadována velikost – průřez – cca 0,3 mm – určení molekulární struktury nových či dosud nepopsaných látek

Rentgenová difraktometrie

* Princip jednoduchého spektrometru



- Úhlová disperze RTG spektrometru

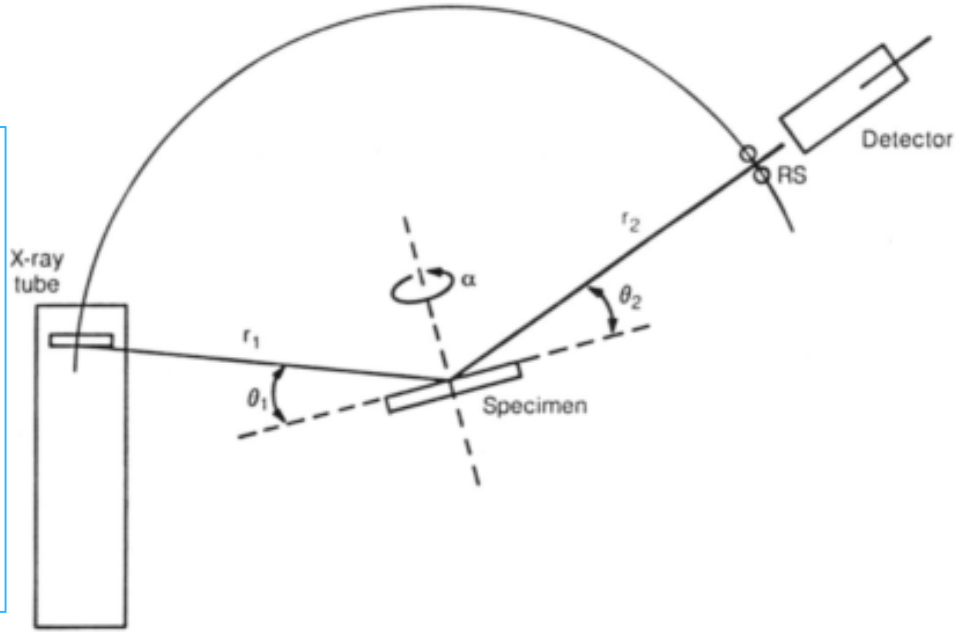
$$\frac{\partial \vartheta}{\partial \lambda} = \frac{n}{2d \cos \vartheta}$$

- přímá úměra k řádu difrakce
- intenzita ovšem klesá s řádem

Rentgenová difraktometrie

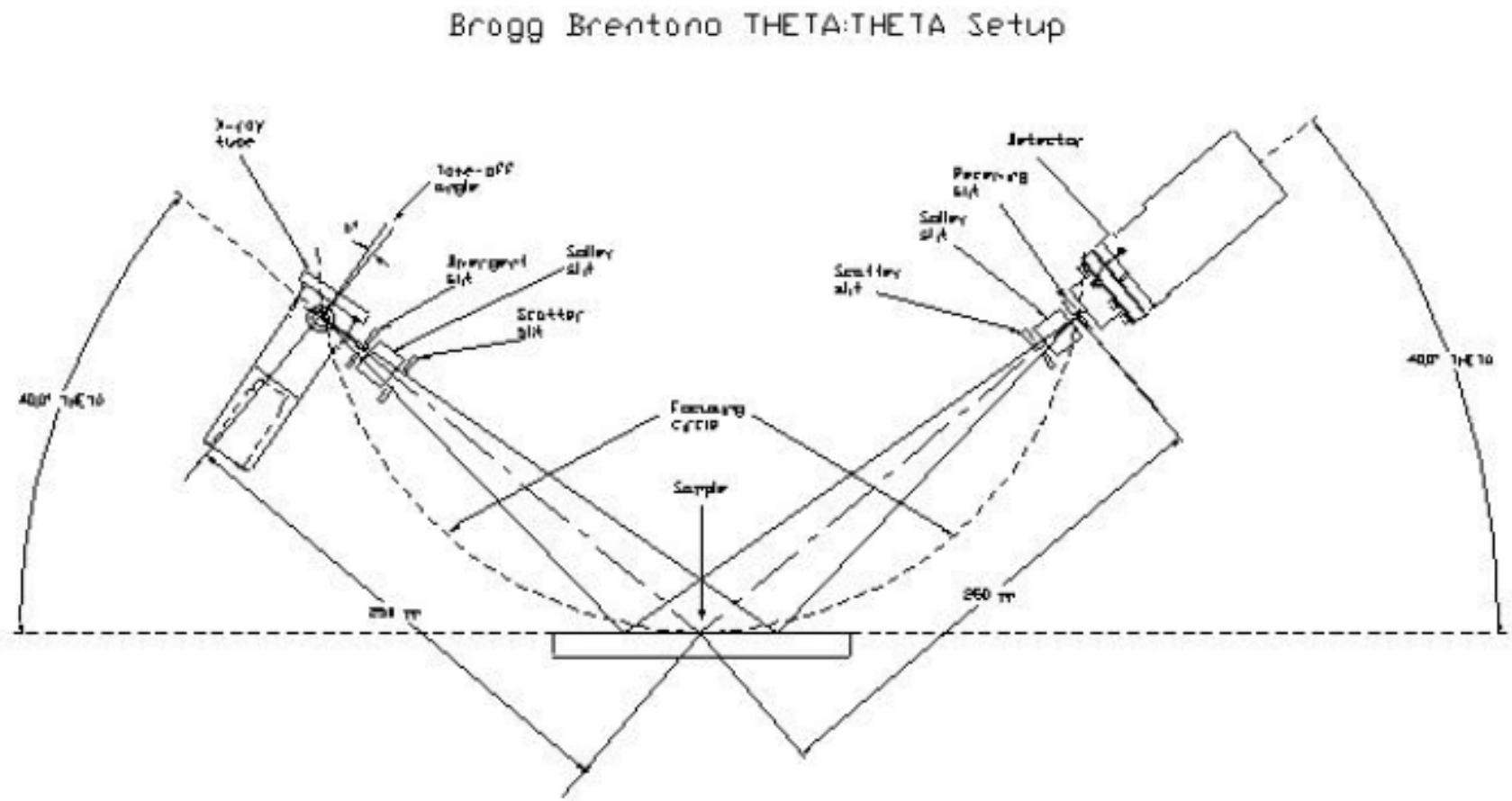
* Obvykle snímána spektra 1. řádu – pouze pro rozlišení detailů spektra vyšších řádů – výrazné prodloužení doby expozice
* Mezní dosažitelné rozlišení určeno rozlišovací schopností přístroje $\lambda/\delta\lambda$
* Bragg-Brentanův difraktometr

For the THETA:2-THETA goniometer, the X-ray tube is stationary, the sample moves by the angle THETA and the detector simultaneously moves by the angle 2-THETA.



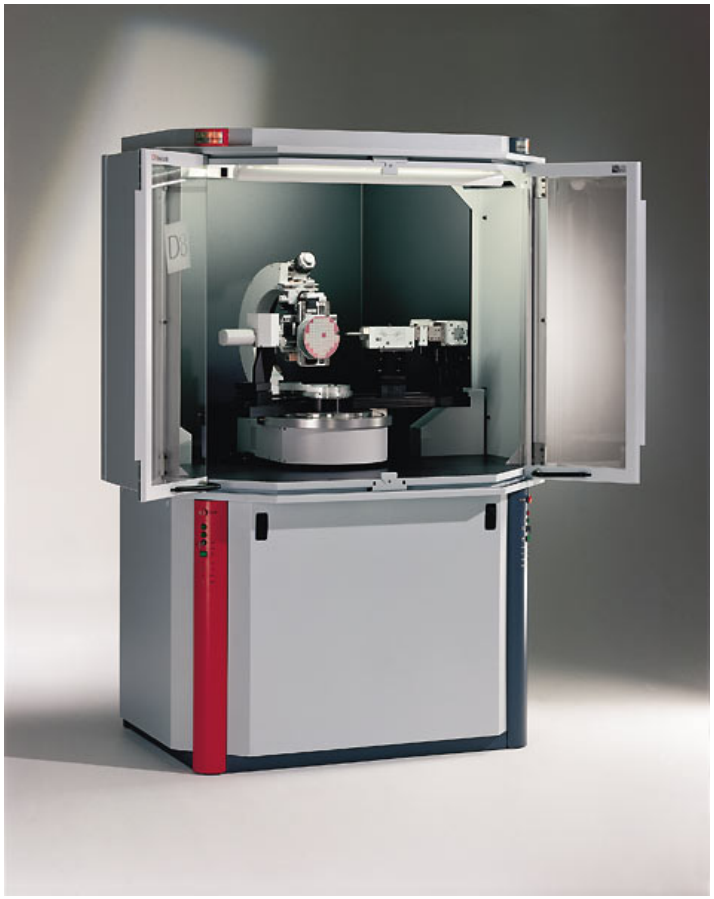
Rentgenová difraktometrie

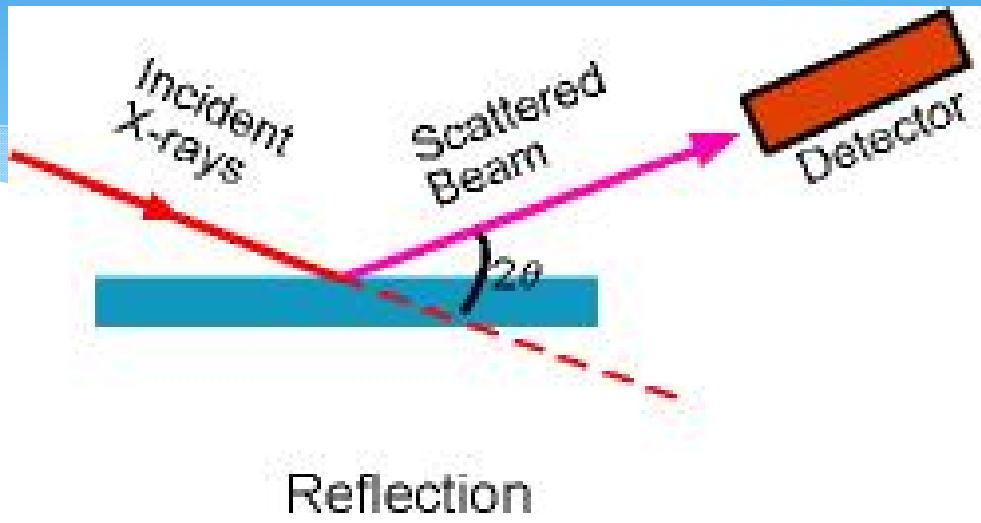
- Bragg-Brentanův difraktometr
- For the THETA:THETA goniometer, the sample is stationary in the horizontal position, the x-ray tube and the detector both move simultaneously over the angular range THETA.



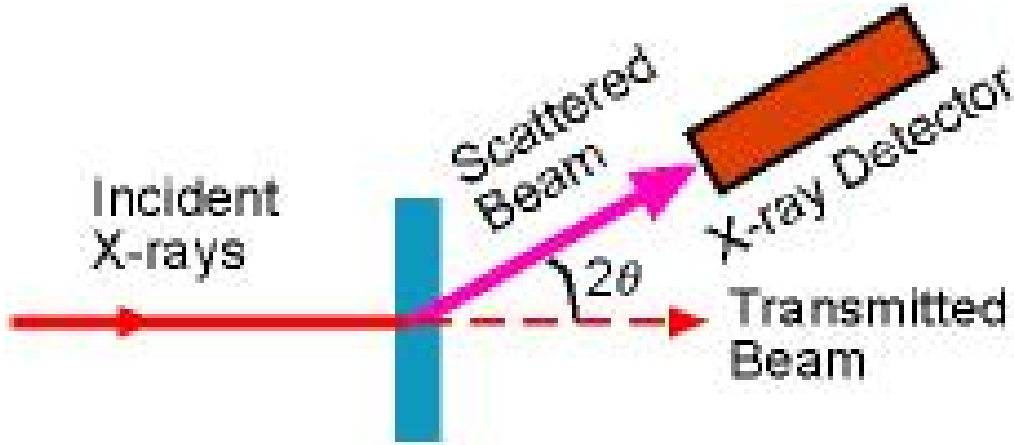
Rentgenová difraktometrie

* **PRÁŠKOVÁ**





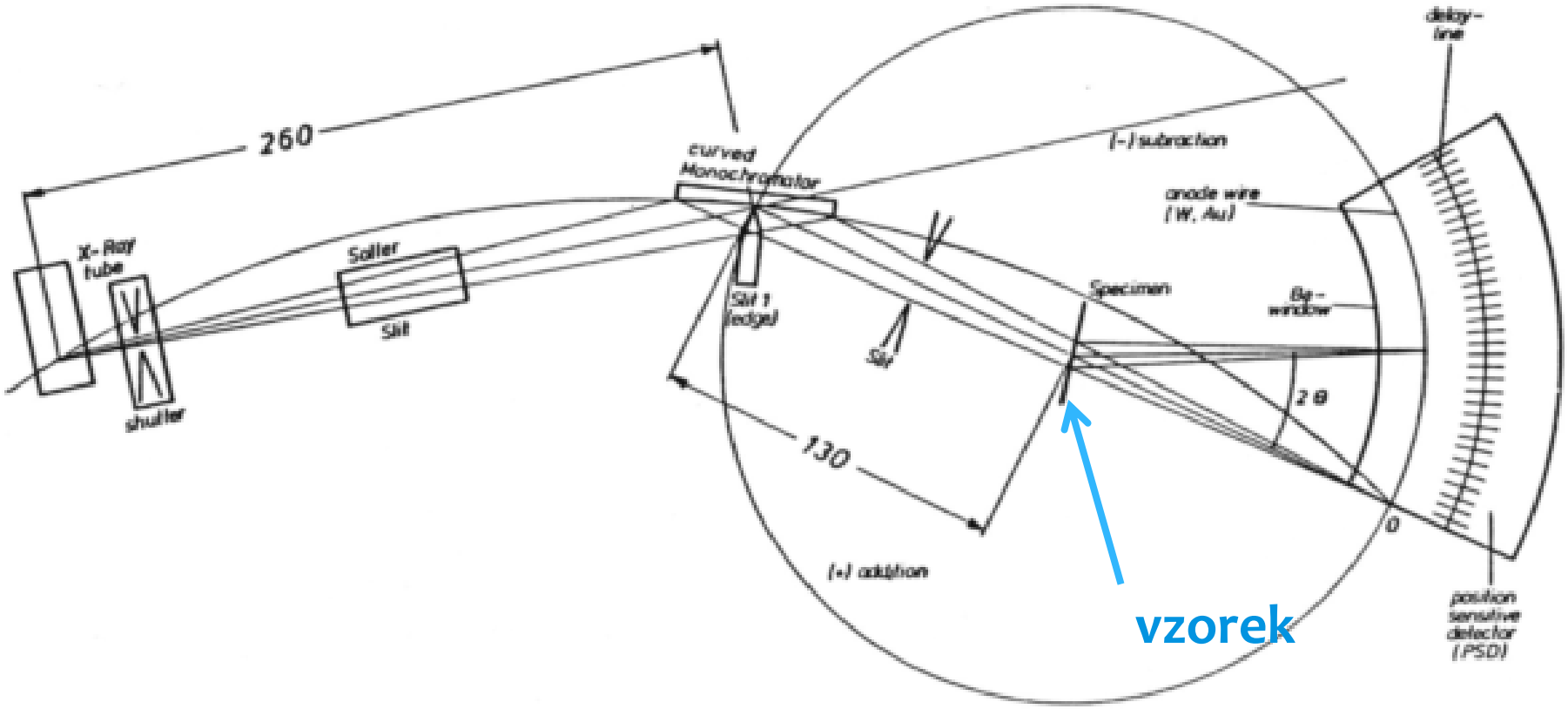
Reflection



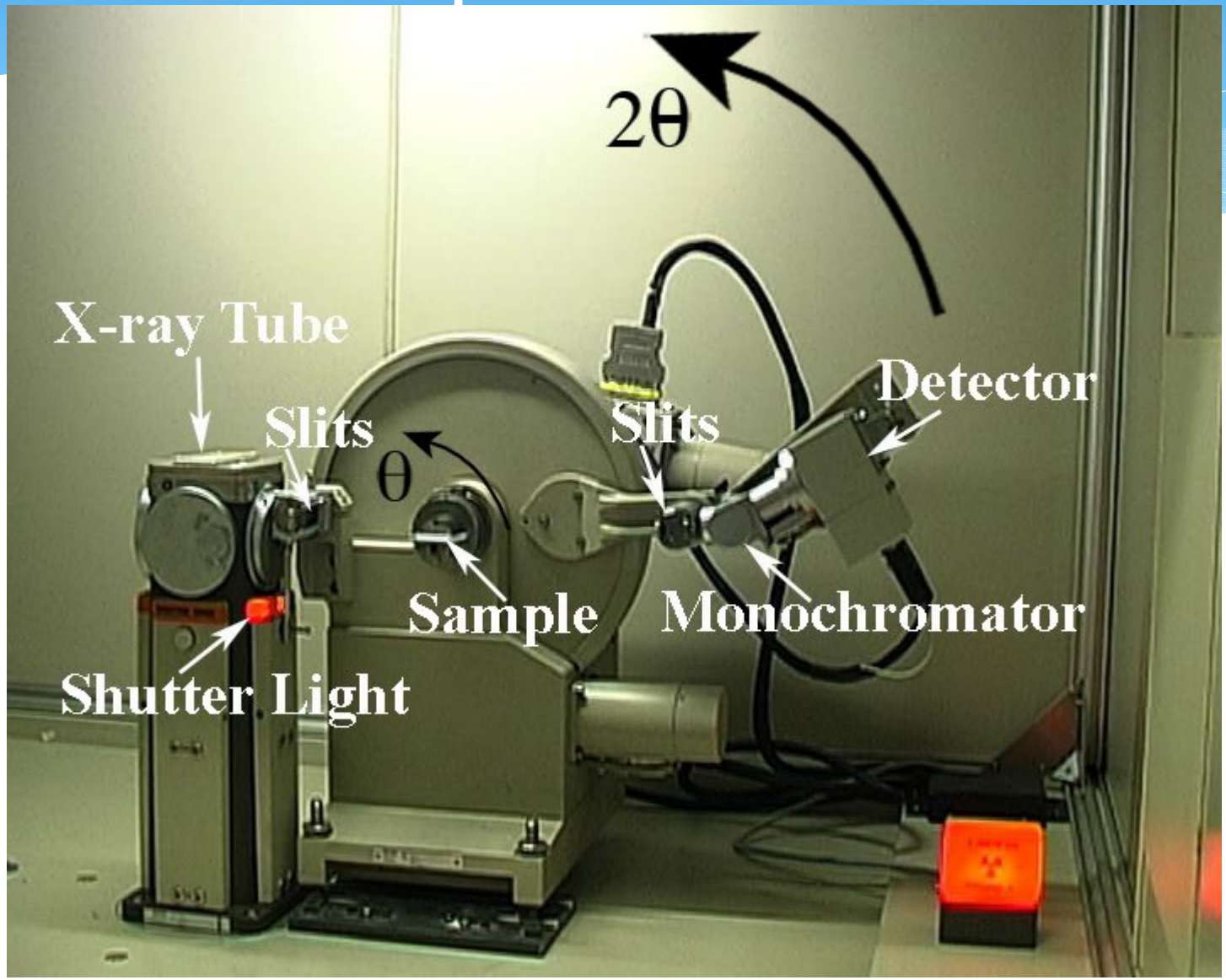
Transmission

Rentgenová difraktometrie

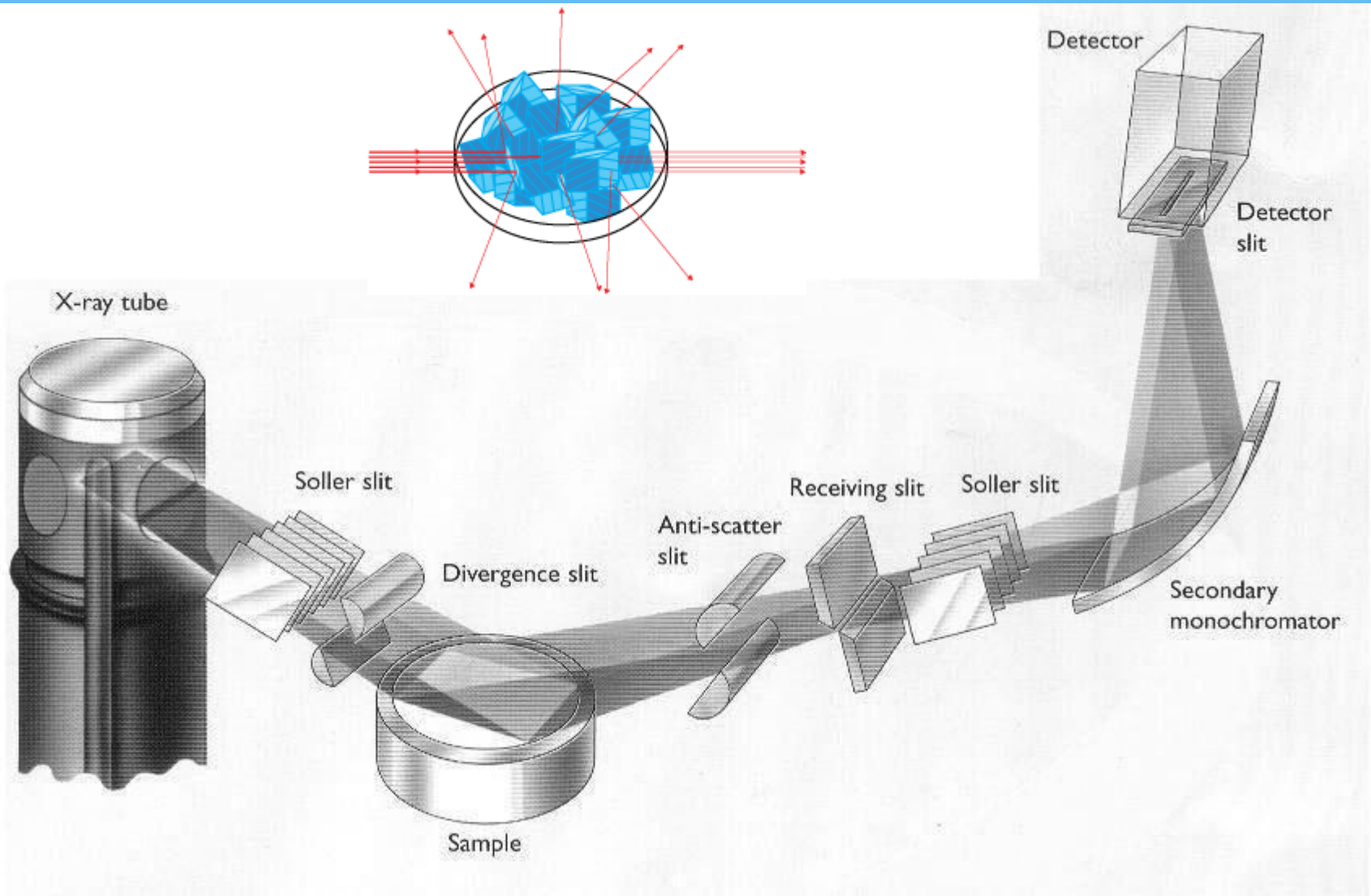
* Transmisní uspořádání difraktometru s primárním monochromátorem (pro práškovou difraktometrii) (obecně monochromátor v primárním či difraktovaném svazku



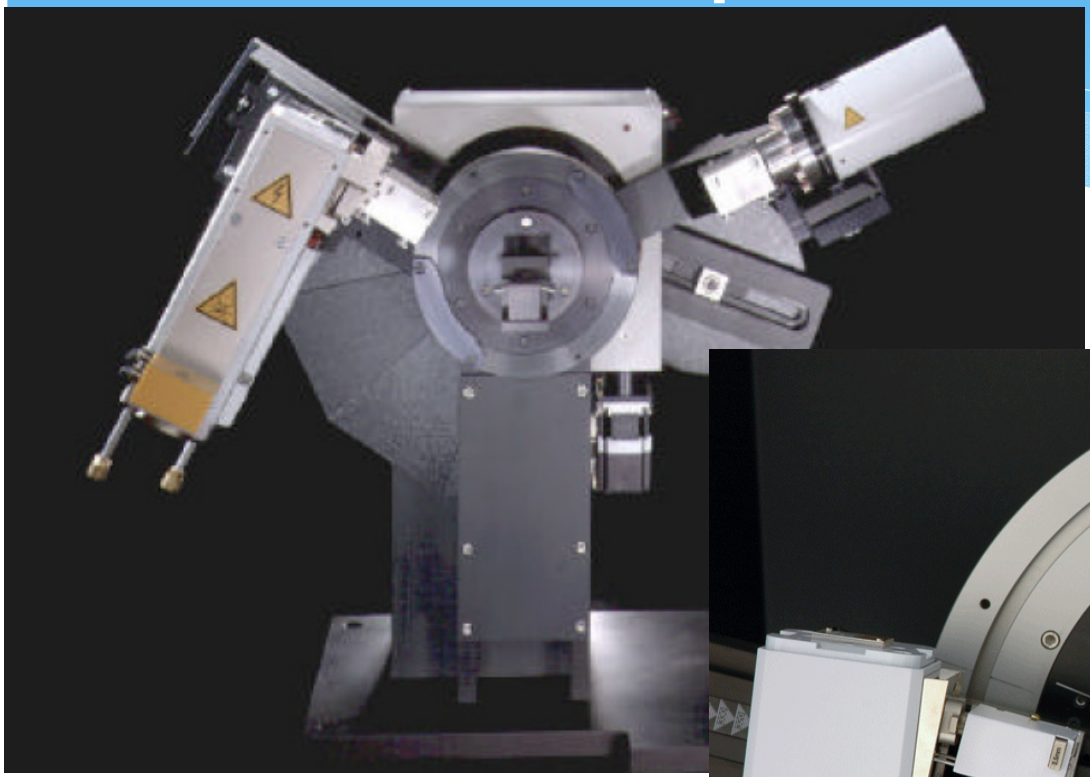
Rentgenová difraktometrie prášková

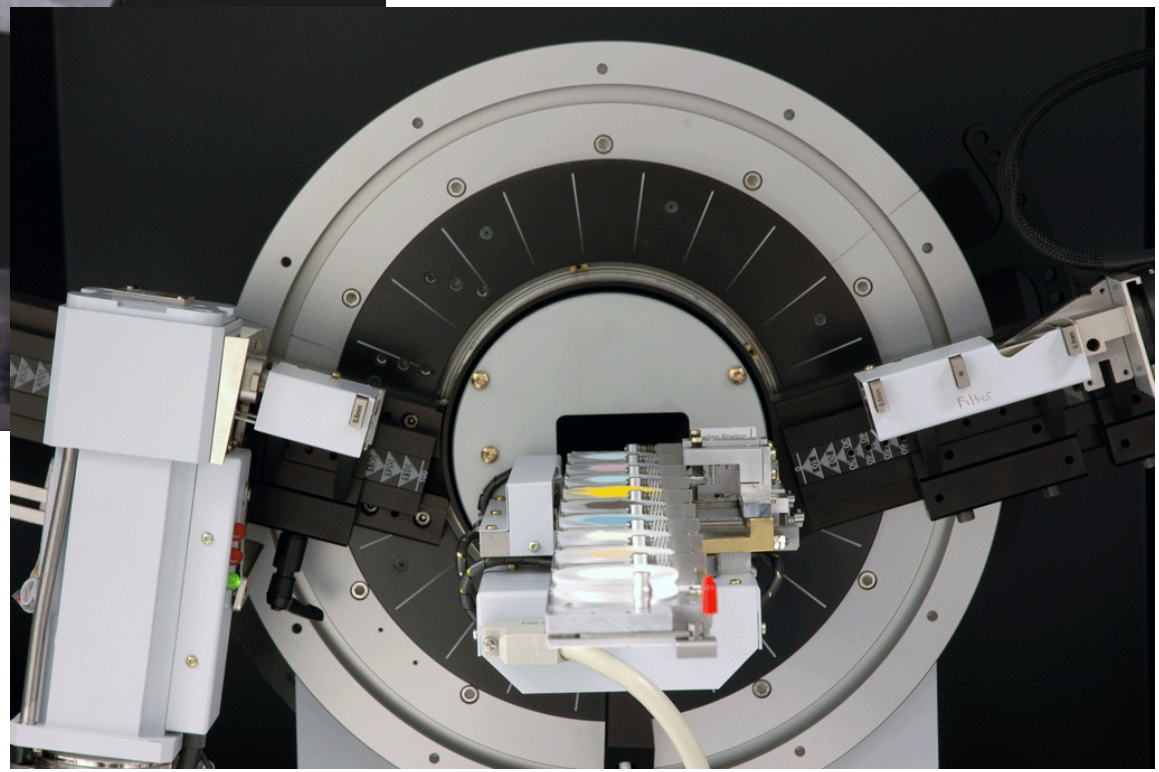


Rentgenová difraktometrie prášková

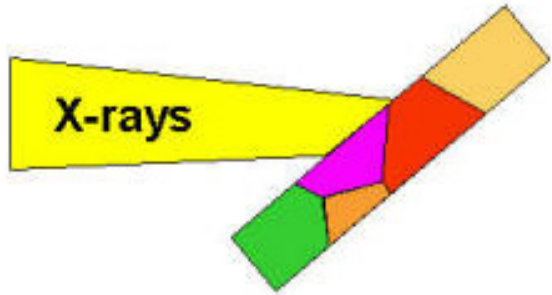


Rentgenová difraktometrie prášková

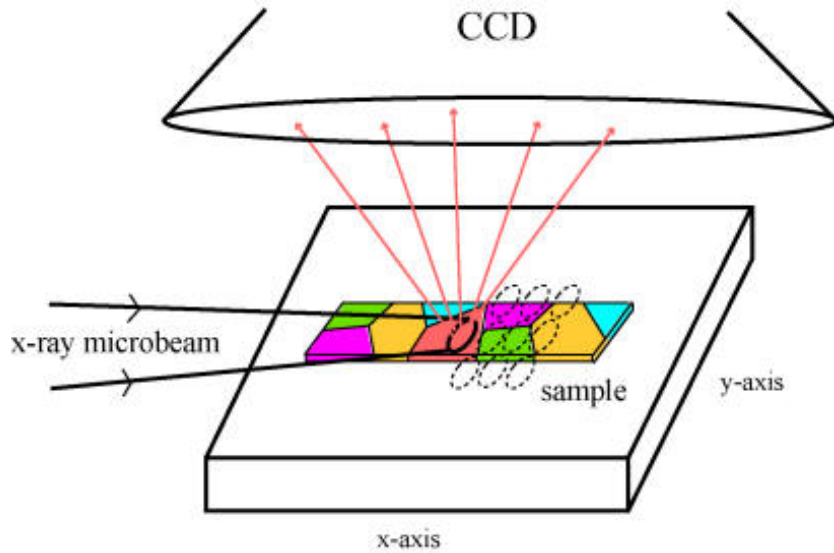




Rentgenová difraktometrie



* Ozařovaná plocha na vzorku – běžně mm^2, pokud se nejedná o mikroanalýzu
* Intenzita ozařování – řádově stovky W/mm^2
* **RTG – mikrodifrakce** – ozařovaná plocha běžně μm^2 i méně (synchrotronové záření) – mikrostruktura materiálů – lokální změny struktury



Rentgenová difraktometrie

* **RTG – mikrodifrakce**

Material analysis with X-ray microdiffraction

F. Friedel*[1], U. Winkler[1], B. Holtz[1], R. Seyrich[2], and H.-J. Ullrich[2]

Cryst. Res. Technol. **40**, No. 1/2, 182 – 187 (2005) / **DOI** 10.1002/crat.200410323

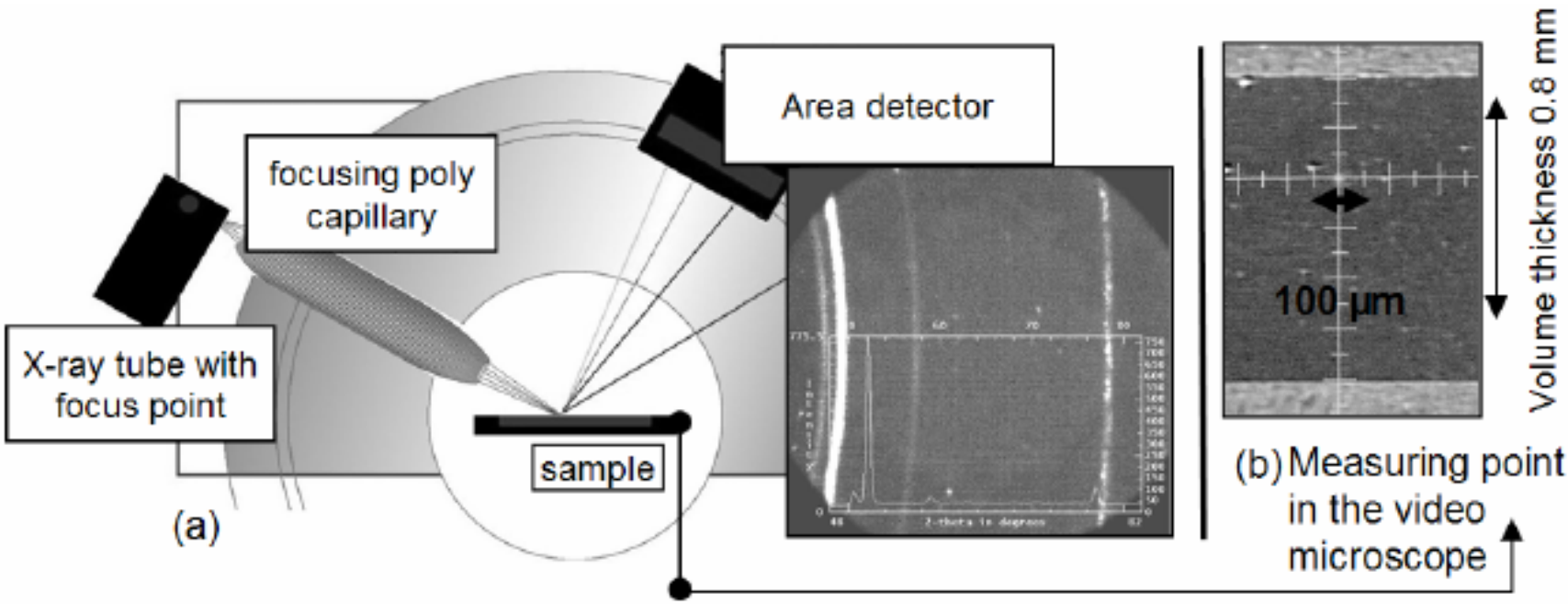


Fig. 2 Principle of X-ray microdiffraction with focusing polycapillary and area detector (source: Bruker AXS) (a), View by the video microscope of the microdiffraction equipment of the embedded and polished cross section (b).

Rentgenová difraktometrie

* **RTG – mikrodifrakce**

Material analysis with X-ray microdiffraction

F. Friedel*[1], U. Winkler[1], B. Holtz[1], R. Seyrich[2], and H.-J. Ullrich[2]

Cryst. Res. Technol. **40**, No. 1/2, 182 – 187 (2005) / **DOI** 10.1002/crat.200410323

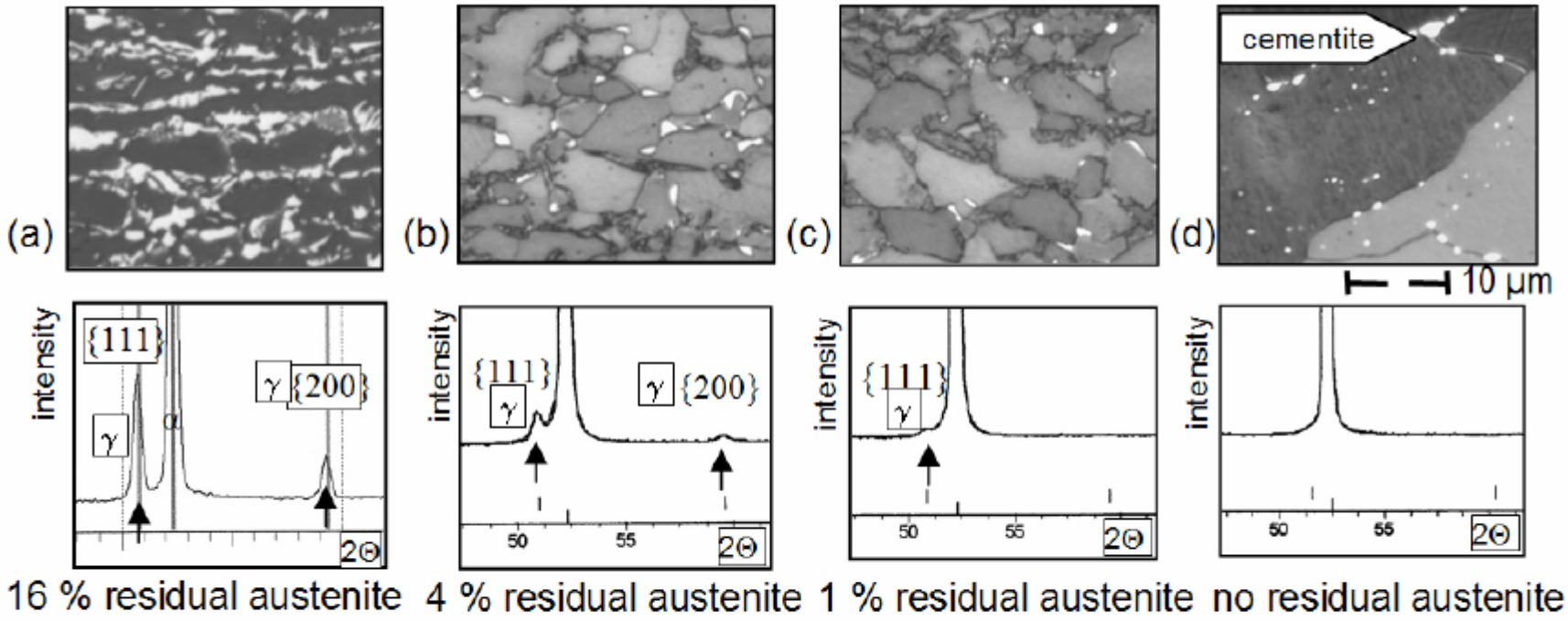
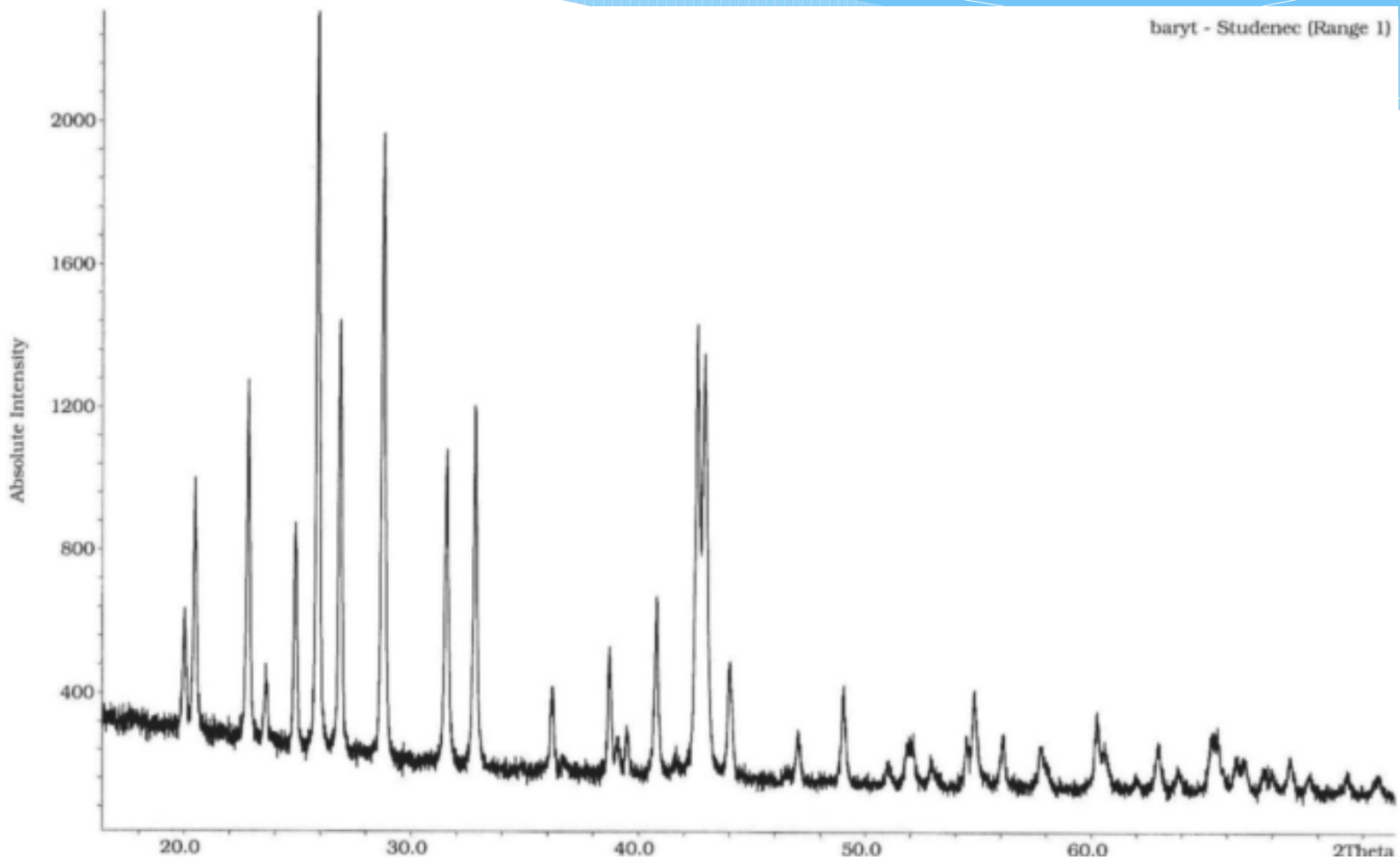


Fig. 3 Measurement of residual austenite in the structure of a RA-steel (a), DP-steel (b) and (c) as well as distinction of the residual austenite as "white phase in the KLEMM etch process" of cementite in a conventional steel (d).

Rentgenová difraktometrie "prášková"

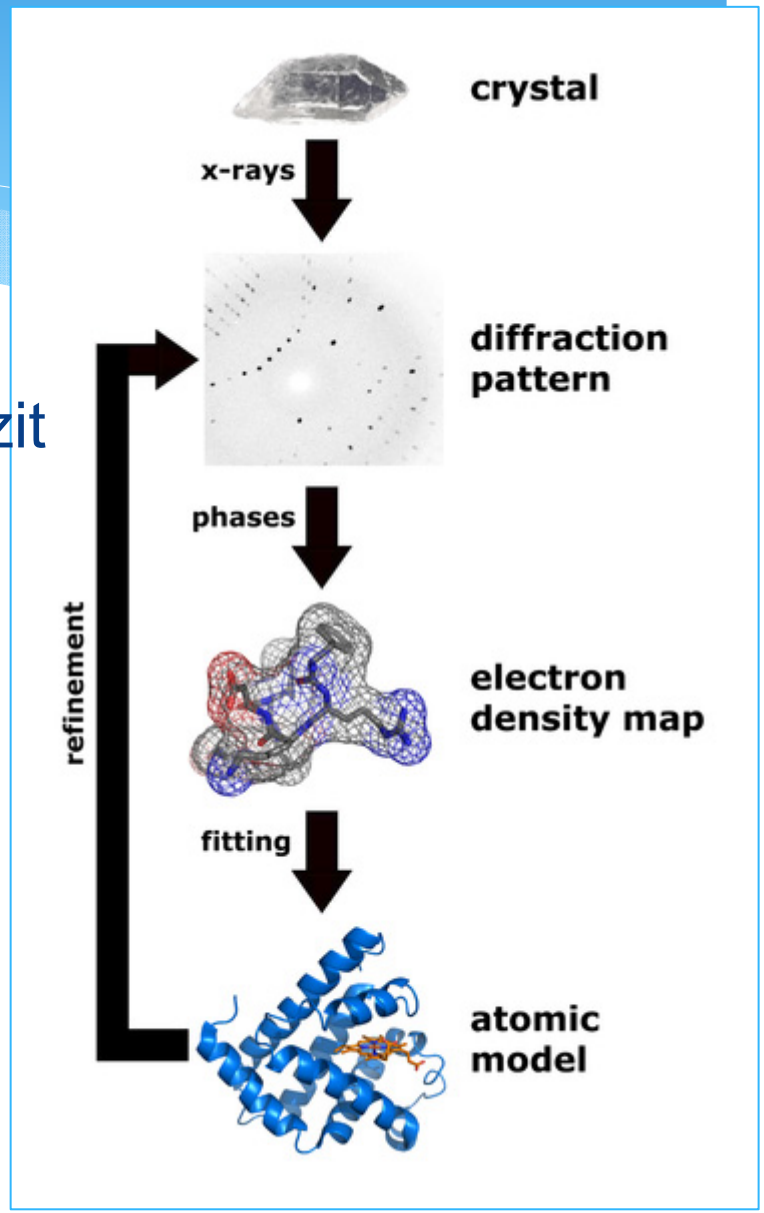
* Difraktogram



Rentgenová difraktometrie

* Kroky analýzy v RTG difraktometrii

* 1) měření difraktogramu
* 2) vyhodnocení - určení poloh a intenzit difrakcí (píků)
* 3) indexování difrakcí (h, k,l)
* 4) parametry základní buňky



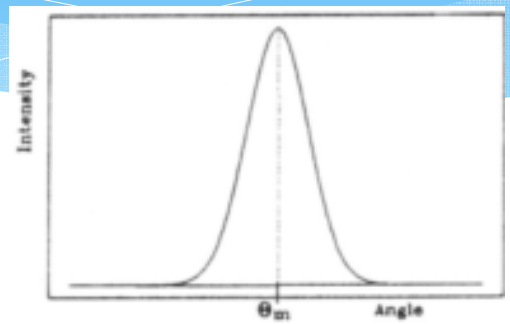
Rentgenová difraktometrie

* Kroky analýzy v RTG difraktometrii
* vyhodnocení - určení poloh a intenzit difrakcí (píků)
* přípravné kroky
* vyhlazení záznamu (proklady metodou nejmenších čtverců)
* odečtení pozadí
* vyhodnocení záznamu 2. derivace

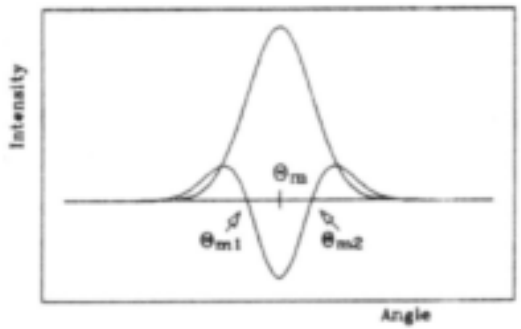
* zhodnocení instrumentálních vlivů (aberací) – instrumentální justace, neistrumentální korekce, metoda vnitřního standardu

Rentgenová difraktometrie

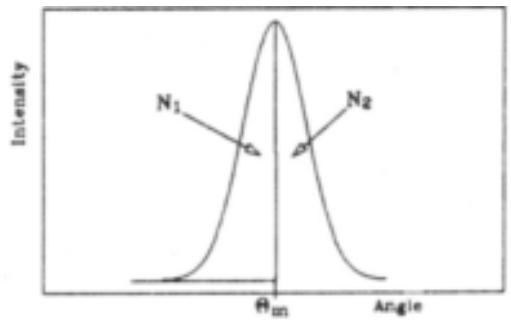
* Kroky analýzy v RTG difraktometrii
* vyhodnocení - určení poloh a intenzit difrakcí (píků)
* maximum intenzity



* střední poloha mezi inflexními body



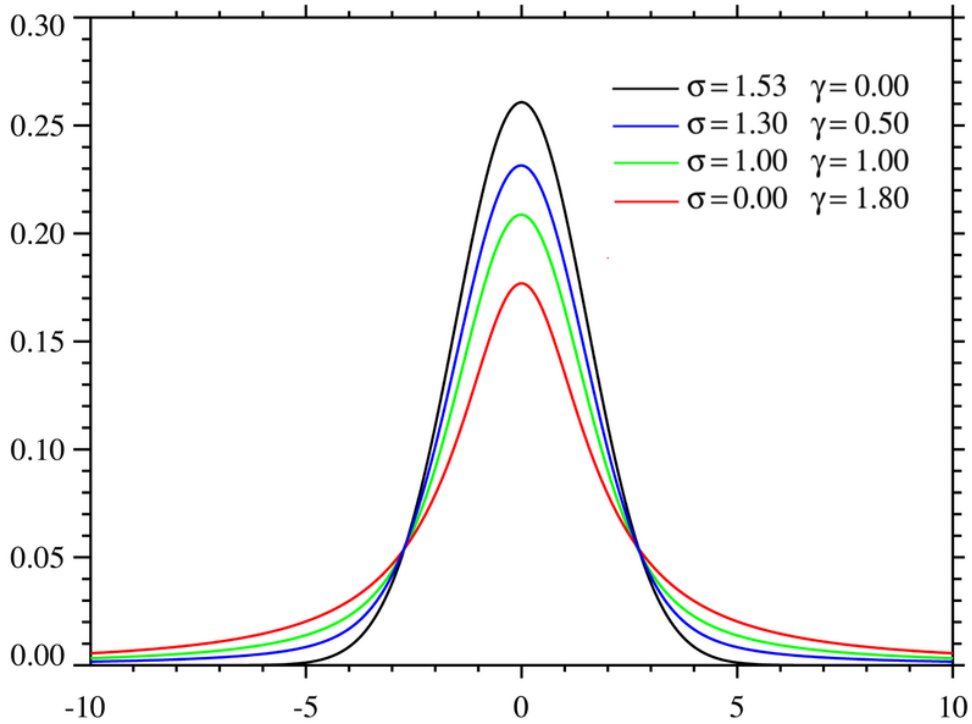
* těžiště difrakční linie
* proložení analytické funkce



Rentgenová difraktometrie

* Vyhodnocení - určení poloh a intenzit difrakcí (píků)
*
* proložení analytické funkce – profilové funkce
* Gaussova
* Lorentzova
* Pearsonova
* Voigtova – konvoluce G & L
* pseudoVoigtova

$$V(x;\sigma,\gamma) = \int_{-\infty}^{\infty} G(x';\sigma)L(x-x';\gamma)\,dx'$$



Plot of the centered Voigt profile for four cases. Each case has a full width at half-maximum of very nearly 3.6. The black and red profiles are the limiting cases of the Gaussian (γ =0) and the Lorentzian (σ =0) profiles respectively.

Rentgenová difraktometrie

- The X-ray diffraction pattern of a pure substance is like a fingerprint of the substance.
- The powder diffraction method is thus ideally suited for characterization and identification of polycrystalline phases.
- Today? about 50,000 inorganic and 25,000 organic single component, crystalline phases, diffraction patterns have been collected and stored on magnetic or optical media as standards. The main use of powder diffraction is to identify components in a sample by a search/match procedure. Furthermore, the areas under the peak are related to the amount of each phase present in the sample.

Rentgenová difraktometrie

- International Center Diffraction Data (ICDD), formerly known as (JCPDS) Joint Committee on Powder Diffraction Standards, is the organization that maintains the database of inorganic and organic spectra. The database is available from diffraction equipment manufacturers or from ICDD direct.
- http://www.icdd.com/
- The database is exhaustive, over 500,000 entries as of 2006; computer algorithms allow rapid peak matching. The organization was founded in 1941 as the Joint Committee on Powder Diffraction Standards (JCPDS).

Rentgenová difraktometrie

- **Aplikace**
- Identifikace – pro krystalické fáze – na základě databáze,
- Studium teplotních změn, vlivu tlaku atp.
- Struktura nových látek
- Míra krystalinity materiálů (polymerů)
- Analýza textury – preferenční orientace v polykrystalických materiálech („preferred crystallographic orientation in a polycrystalline material“)

Rentgenová difraktometrie

Anatase R060277 - RRUFF...

http://rruff.info/Anatase/R060277

Zadejte hledaný text

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RRUFF

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Anatase R060277

Browse S

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Name: Anatase
RRUFF ID: R060277
Ideal Chemistry: TiO_2
Locality: Taftan, near Dalbandi, Baluchistan Province, Pakistan
Source: Herb Obodda 064 [view label]
Owner: RRUFF
Description: Dark brown tetragonal tabular crystals
Status: The identification of this mineral is confirmed by single-crystal X-ray diffraction and c analysis.

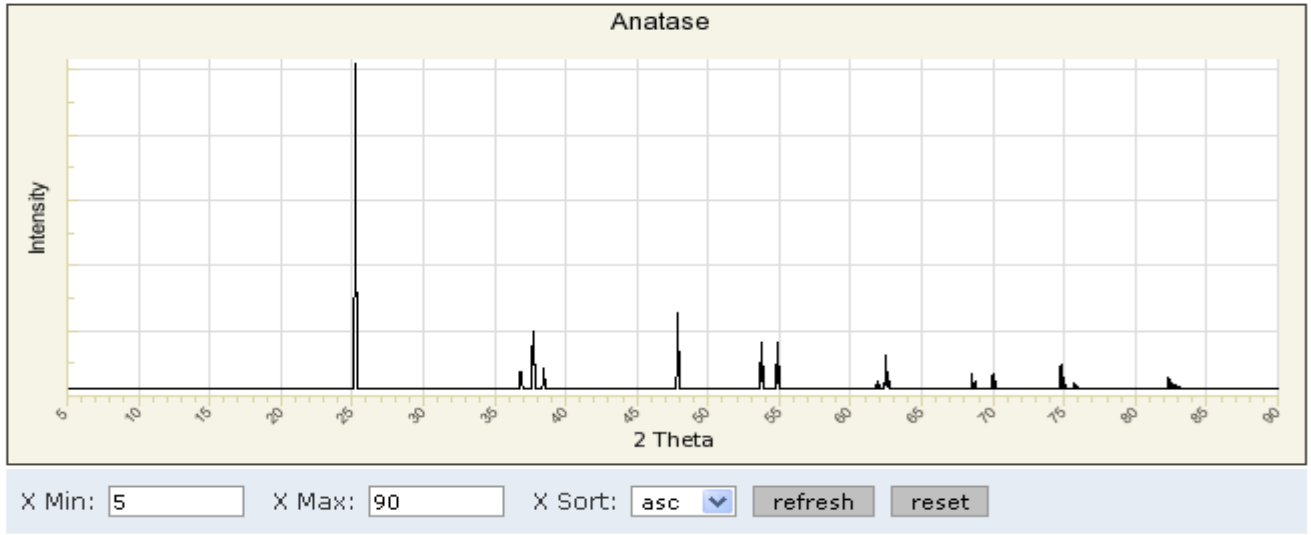
Quick search: [All Anatase samples (2)]

POWDER DIFFRACTION

RRUFF ID: R060277.9
Sample Description: Single crystal, powder profile is calculated
Cell Refinement Output: **a:** 3.799(2)Å **b:** 3.799(2)Å **c:** 9.539(6)Å
alpha: 90° **beta:** 90° **gamma:** 90° **Volume:** 137.67(5) **Crystal System:** tetragonal

DOWNLOADS:

- DIF File
- X-ray Data (XY - RAW) RRUFF File



X Min: 5 X Max: 90 X Sort: asc refresh reset

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Anatase R060277 - RRUFF...

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Anatase R060277

Browse S

<< Previous | Back to Search Res

Name: Anatase
RRUFF ID: R060277
Ideal Chemistry: TiO_2
Locality: Taftan, near Dalbandi, Baluchistan Province, Pakistan

RAMAN SPECTRUM

RRUFF ID: R060277.3

Sample Description: Sample is oriented and mounted on a pin

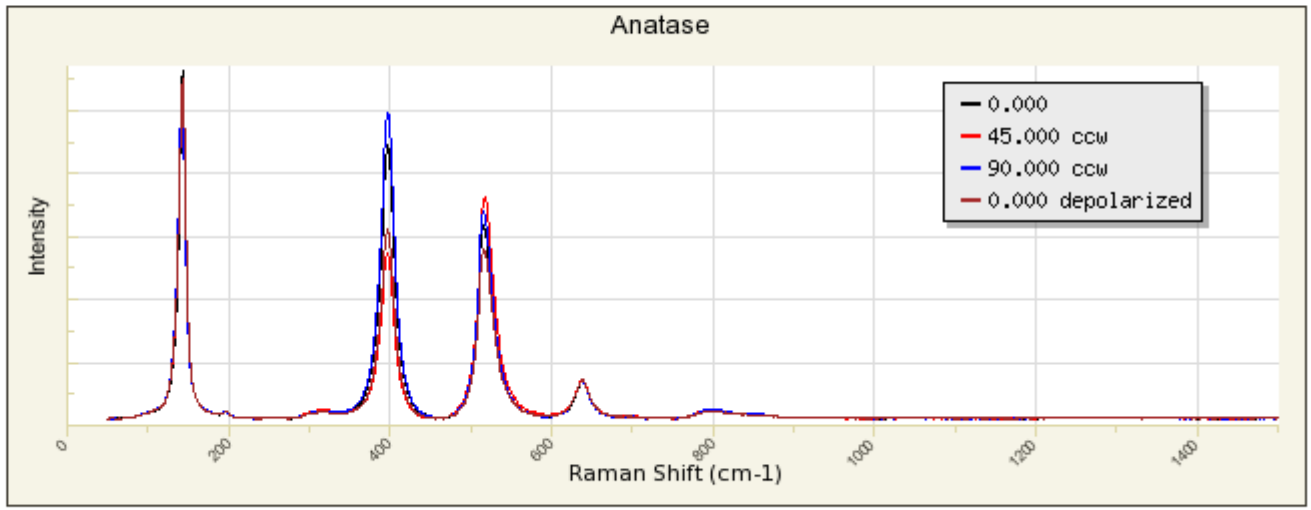
Pin ID: L01480

Orientation: Laser parallel to **c*** (0 0 1). Fiducial mark perpendicular to laser is parallel to [1 1 0].

DOWNLOADS:

To download sample data, please select a specific orientation angle.

Direction of polarization of laser relative to fiducial mark: all data



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Rentgenová difraktometrie

Yttrium aluminum garnet - ... | Yttriumaluminumgarnet__X...

http://rruff.info/yttrium%20aluminum%20garnet/display=default/

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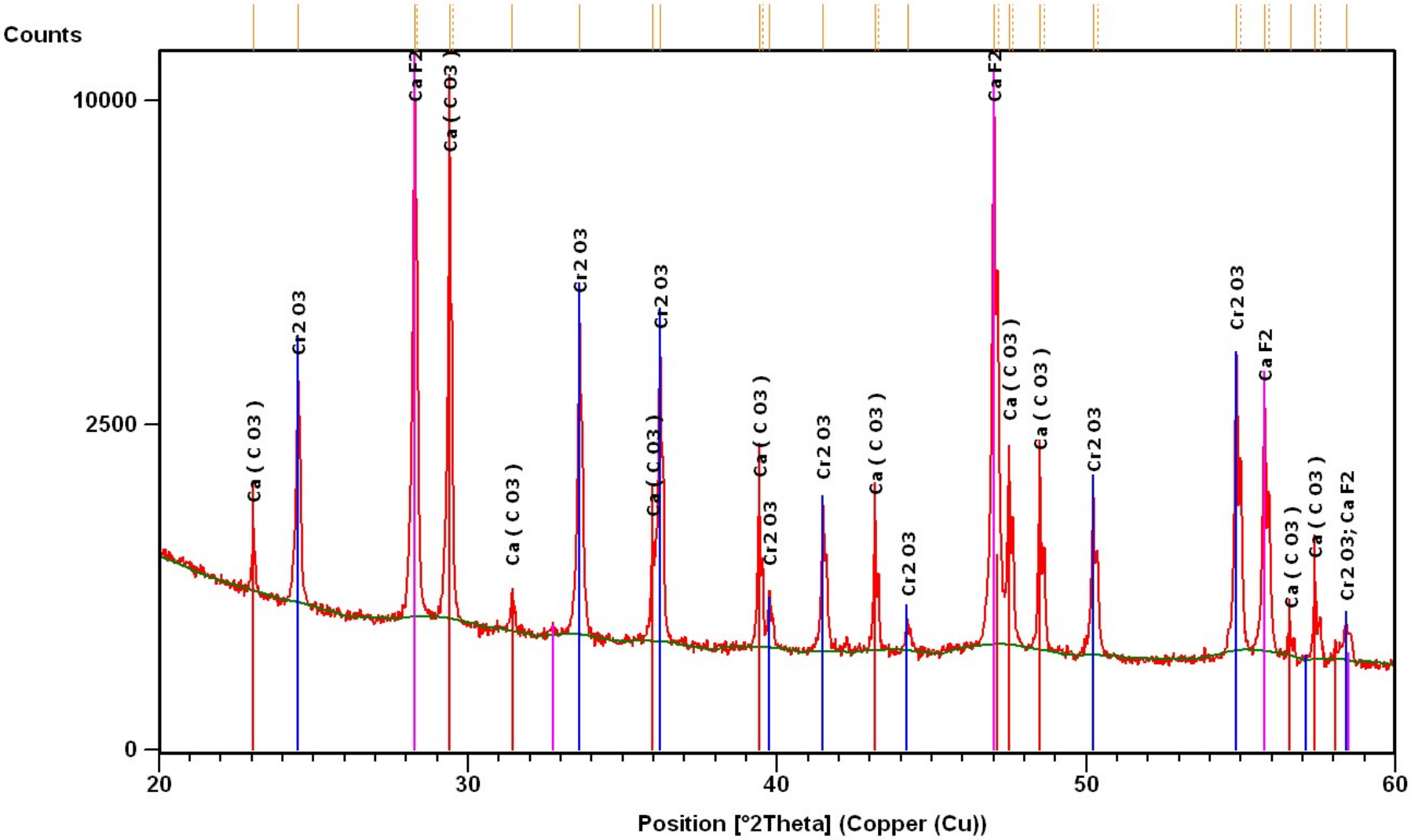
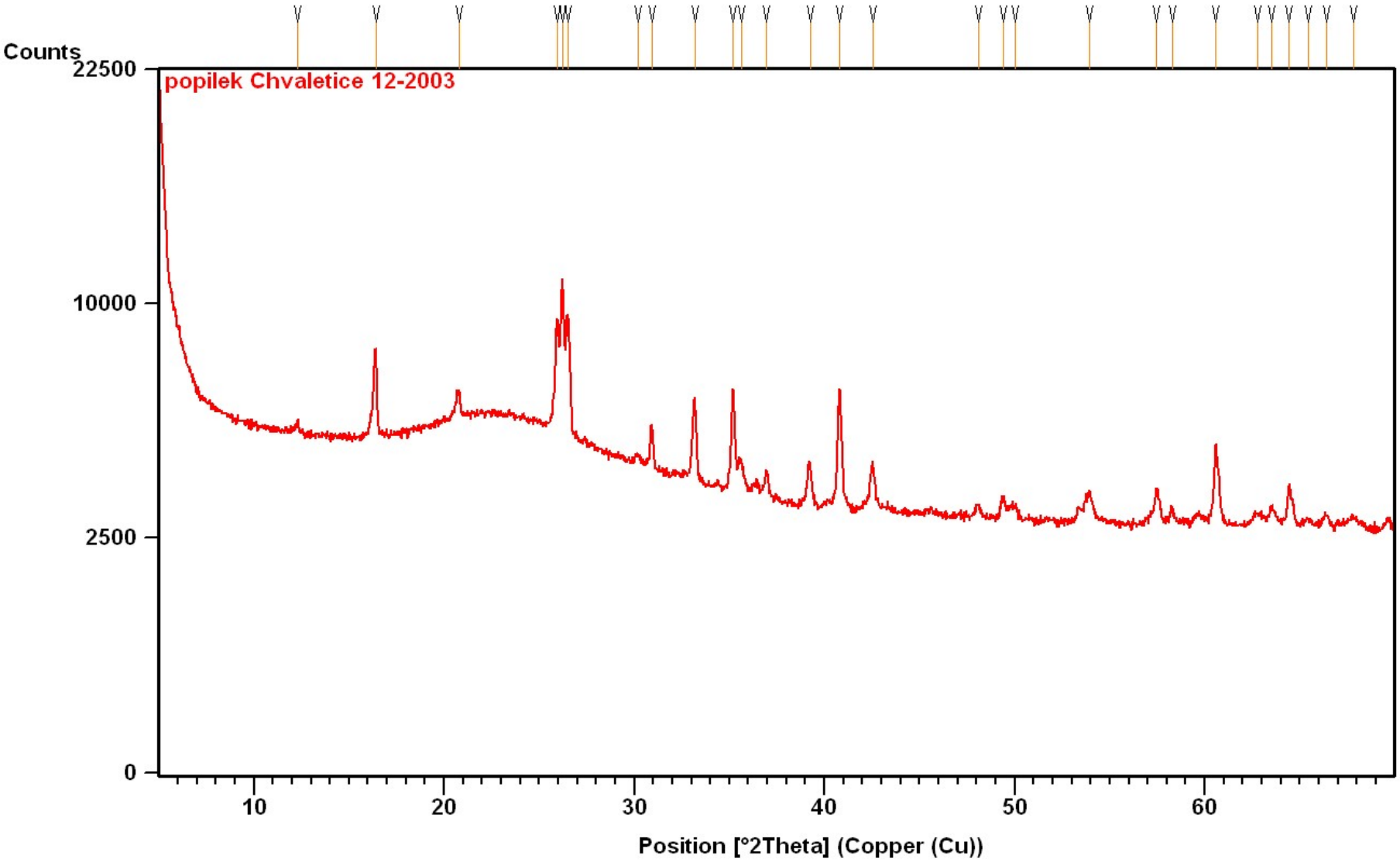
Yttrium aluminum garnet X090003

Name: Yttrium aluminum garnet
RRUFF ID: X090003
Ideal Chemistry: $Y_3Al_2(AlO_4)_3$
Locality: Synthetic
Source: Gemological Institute of America 15735
Owner: GIA
Description: Faceted colorless gemstone, 1.42 ct
Status: The identification of this mineral has only been confirmed by single-crystal X-ray diffraction.

Difrakční záznam směsi krystalických fází



Difrakční záznam směsi krystalické a amorfní fáze



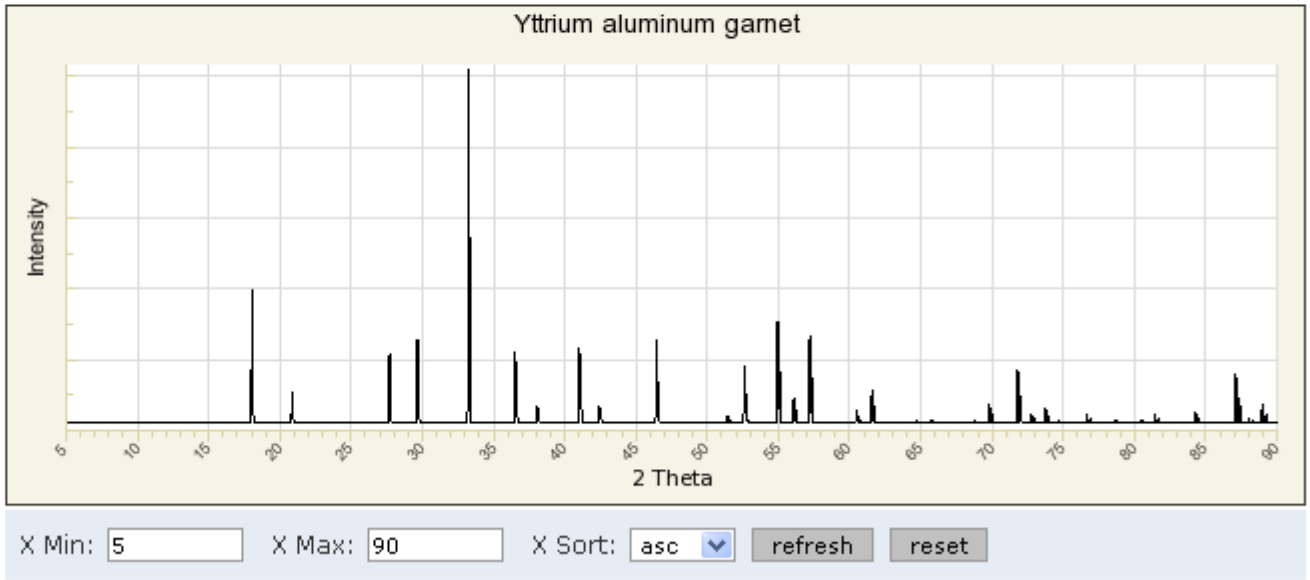
Rentgenová difraktometrie

POWDER DIFFRACTION

RRUFF ID: X090003.9
Sample Description: Single crystal, powder profile is calculated
Cell Refinement Output: **a:** 12.041(7)Å **b:** 12.041(7)Å **c:** 12.041(7)Å
alpha: 90° **beta:** 90° **gamma:** 90° **Volume:** 1745.7(1) **Crystal System:** cubic

DOWNLOADS:

- DIF File
- X-ray Data (XY - RAW)
- RRUFF File



http://rruff.info/yttrium%20aluminum%20garnet/display=default/

Rentgenová difraktometrie

Non-destructive analysis of cultural heritage artefacts from Andalusia, Spain, by X-ray diffraction with Göbel mirrors

A. Duran*, L.K. Herrera, M.C. Jimenez de Haro, A. Justo, J.L. Perez-Rodriguez

Materials Science Institute of Seville (CSIC-Seville University), Avda Americo Vespucio, s/n. 41092 Seville, Spain

Talanta 76 (2008) 183–188

GradedMultilayer Optics ("Göbel-Mirrors") have proved as very useful beam conditions for parallel-beam diffraction without sampling.

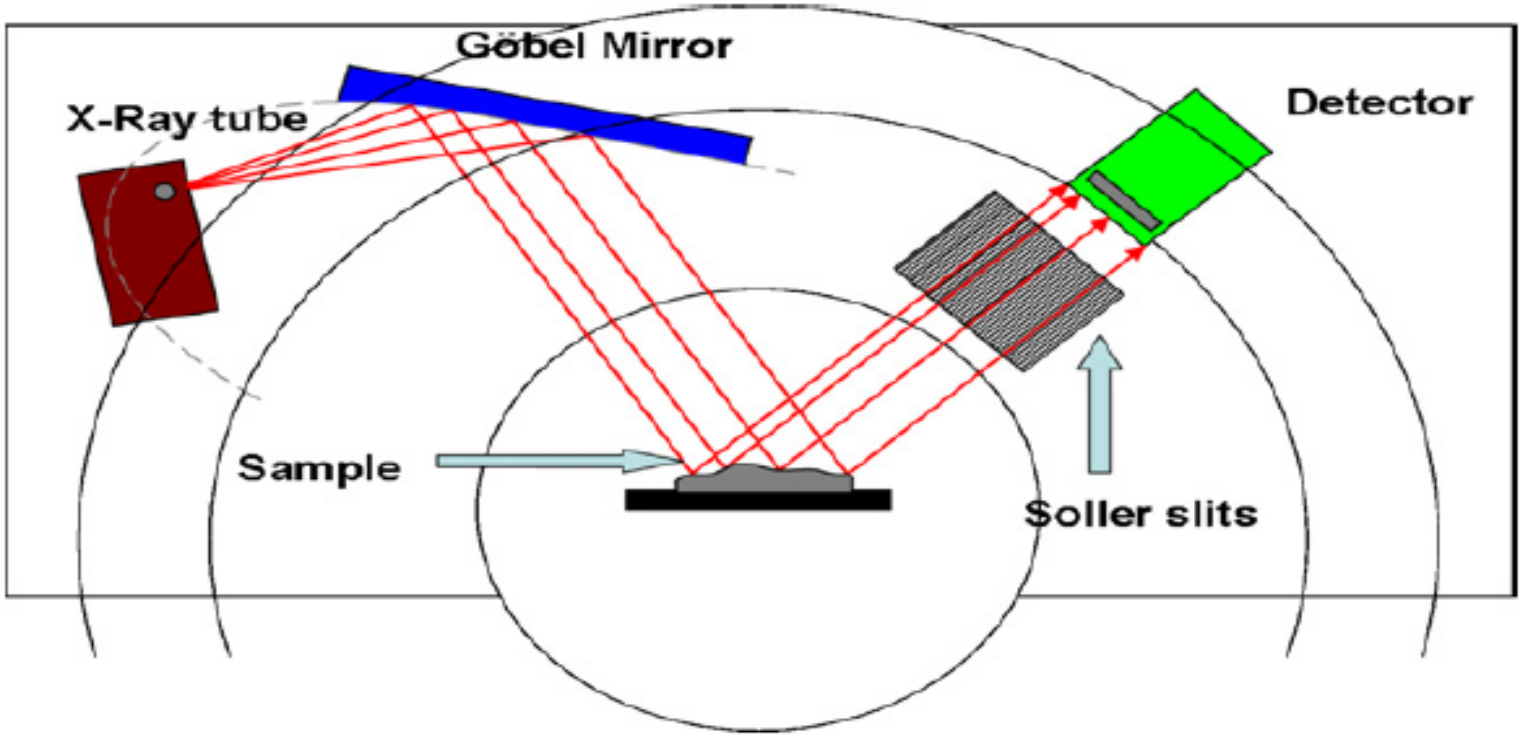


Fig. 1. Experimental procedure for non-destructive analysis by X-ray diffraction with Göbel mirrors of artefacts belonging to cultural heritage.

Rentgenová difraktometrie

Non-destructive analysis of cultural heritage artefacts from Andalusia, Spain, by X-ray diffraction with Göbel mirrors

A. Duran*, L.K. Herrera, M.C. Jimenez de Haro, A. Justo, J.L. Perez-Rodriguez

Materials Science Institute of Seville (CSIC-Seville University), Avda Americo Vespucio, s/n. 41092 Seville, Spain

Talanta 76 (2008) 183–188

The "Göbel-Mirrors" are a **device, based on a layered crystal**, which, mounted on a D-5000 Siemens diffractometer, transforms the primary divergent X-ray beam into a **highly brilliant, parallel beam**. If dimensions of an object are adequate (up to 60cm in bulk), it can be directly analyzed by XRD, without sampling. **Even a rough, irregular surface, both on flat and bent objects, is suitable for the analysis.**

The XRD analysis using Göbel mirrors is therefore, totally nondestructive and very useful to study artefacts from Cultural Heritage [5–7]. It can be obviously very adaptable to study the surfaces of these artefacts, giving information of **degradation and corrosion processes** and information about **pigments, ceramics, metals, patinas, crusts**, etc., used to manufactured artworks.

Rentgenová difraktometrie monokrystal

Single-crystal X-ray Diffraction is a non-destructive analytical technique which provides detailed information about the internal lattice of crystalline substances, including unit cell dimensions, bond-lengths, bond-angles, and details of site-ordering.

Directly related is single-crystal refinement, where the data generated from the X-ray analysis is interpreted and refined to obtain the crystal structure.

Rentgenová difraktometrie monokrystal

In an X-ray diffraction measurement, a crystal is mounted on a goniometer and gradually rotated while being bombarded with X-rays, producing a diffraction pattern of regularly spaced spots known as *reflections*.
The two-dimensional images taken at different rotations are converted into a three-dimensional model of the density of electrons within the crystal using the mathematical method of Fourier transforms, combined with chemical data known for the sample.
Poor resolution (fuzziness) or even errors may result if the crystals are too small, or not uniform enough in their internal makeup.

Rentgenová difraktometrie monokrystal

The crystal scatters the X-rays into a pattern of spots or reflections that can be observed on a screen behind the crystal. The relative intensities of these spots provide the information to determine the arrangement of molecules within the crystal in atomic detail.
The intensities of these reflections may be recorded with photographic film, an area detector or with a charge-coupled device (CCD) image sensor.
The peaks at small angles correspond to low-resolution data, whereas those at high angles represent high-resolution data; thus, an upper limit on the eventual resolution of the structure can be determined from the first few images.

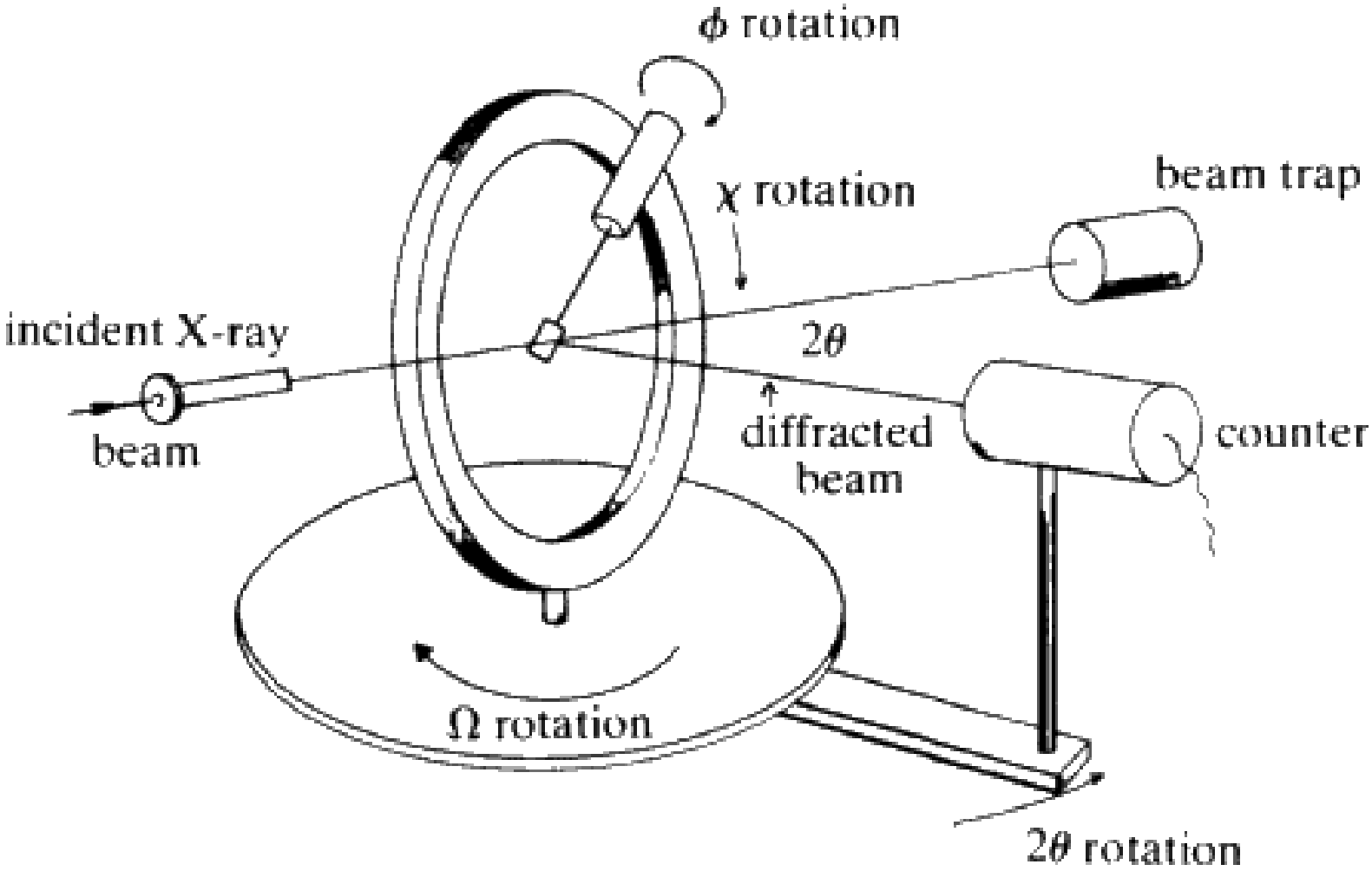
Rentgenová difraktometrie monokrystal

■ an X-ray source consisting of a high-stability X-ray generator, a copper or molybdenum target X-ray tube, a tube shield with associated shutters, attenuators and safety interlocks, a monochromator or X-ray mirror system, and an
incident-beam collimator;
■ a three- or four-circle goniometer system that allows the specimen to be precisely oriented in any position while remaining in the X-ray beam;
■ a video camera or microscope for aligning the specimen and indexing crystal faces;
■ a CCD-based two-dimensional X-ray detector system;
■ a low-temperature attachment for cooling the specimen during data collection;
■ a microprocessor-based interface module that receives commands from a host computer and carries out all real-time instrument control functions to drive goniometer motors, monitor the detector system, open and close the shutter and monitor collision sensors and safety interlocks;

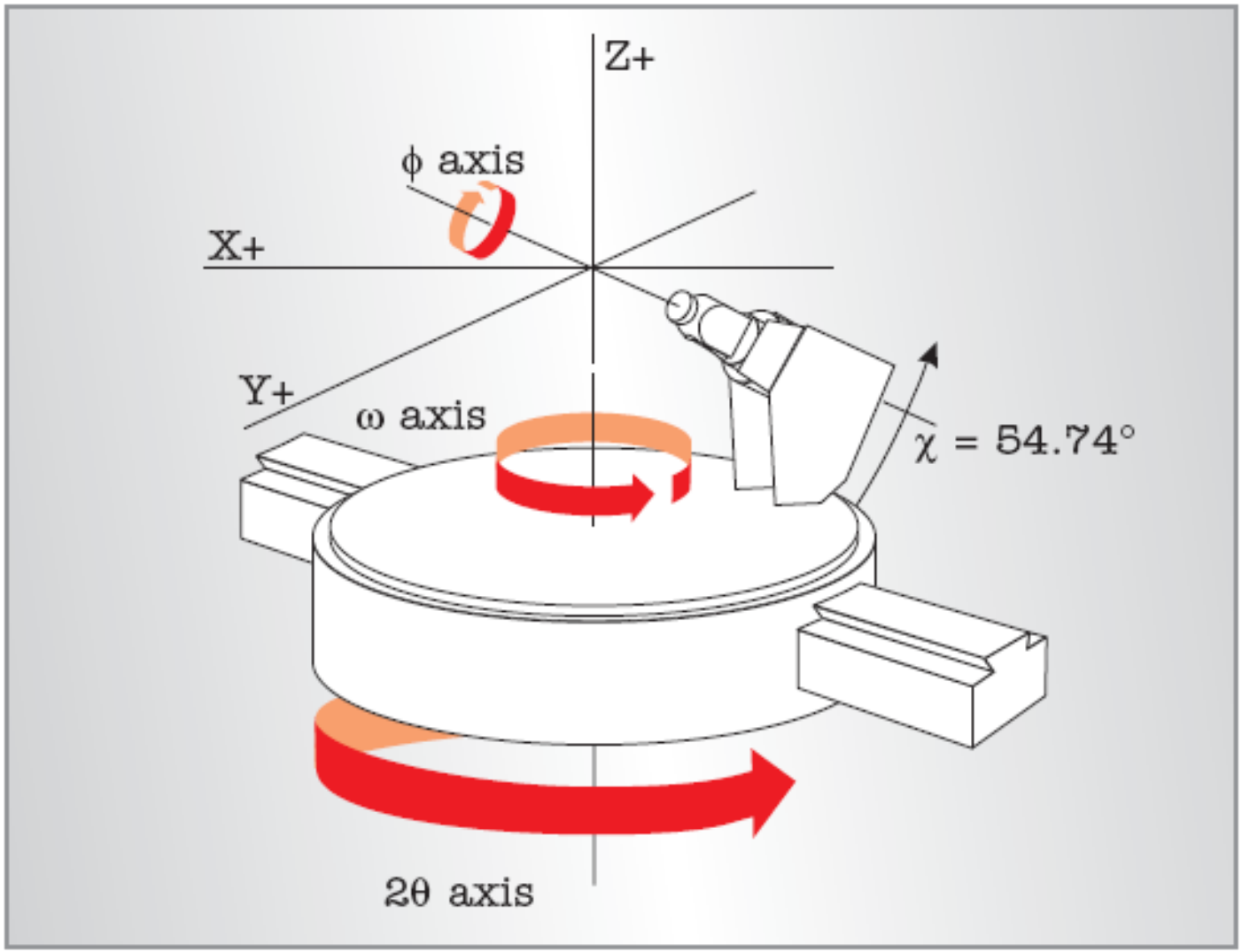
Rentgenová difraktometrie monokrystal

The mounted crystal is irradiated with a beam of monochromatic X-rays.
The brightest and most useful X-ray sources are synchrotrons; their much higher luminosity allows for better resolution.
They also make it convenient to tune the wavelength of the radiation.
Synchrotrons are generally national facilities, each with several dedicated beamlines where data is collected around the clock, seven days a week.

Rentgenová difraktometrie monokrystal



Rentgenová difraktometrie monokrystal



Rentgenová difraktometrie monokrystal

Rentgenová difraktometrie monokrystal

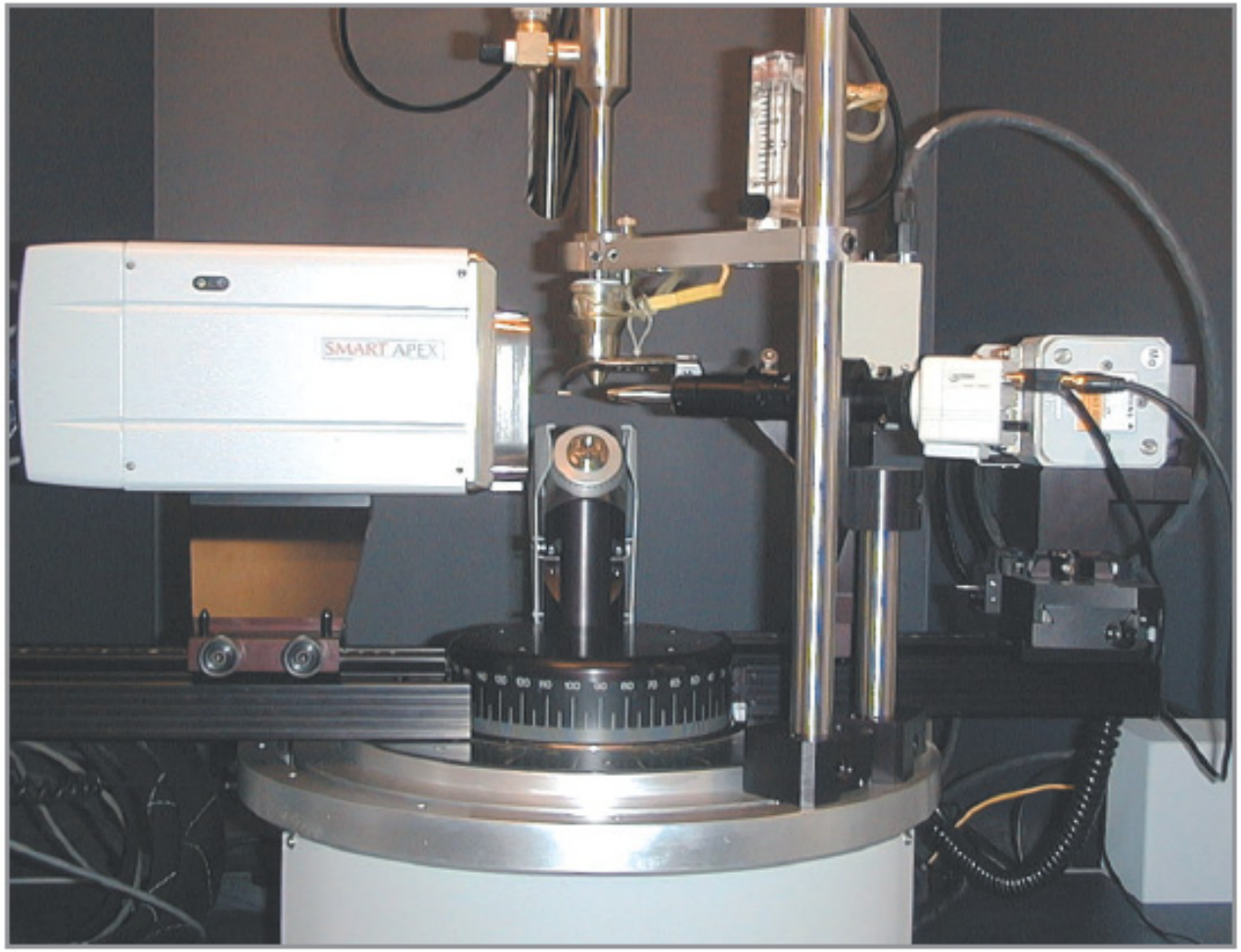


Figure 7. A commercial CCD-based single-crystal X-ray diffractometer system (courtesy of Bruker AXS Inc.)

Rentgenová difraktometrie monokrystal

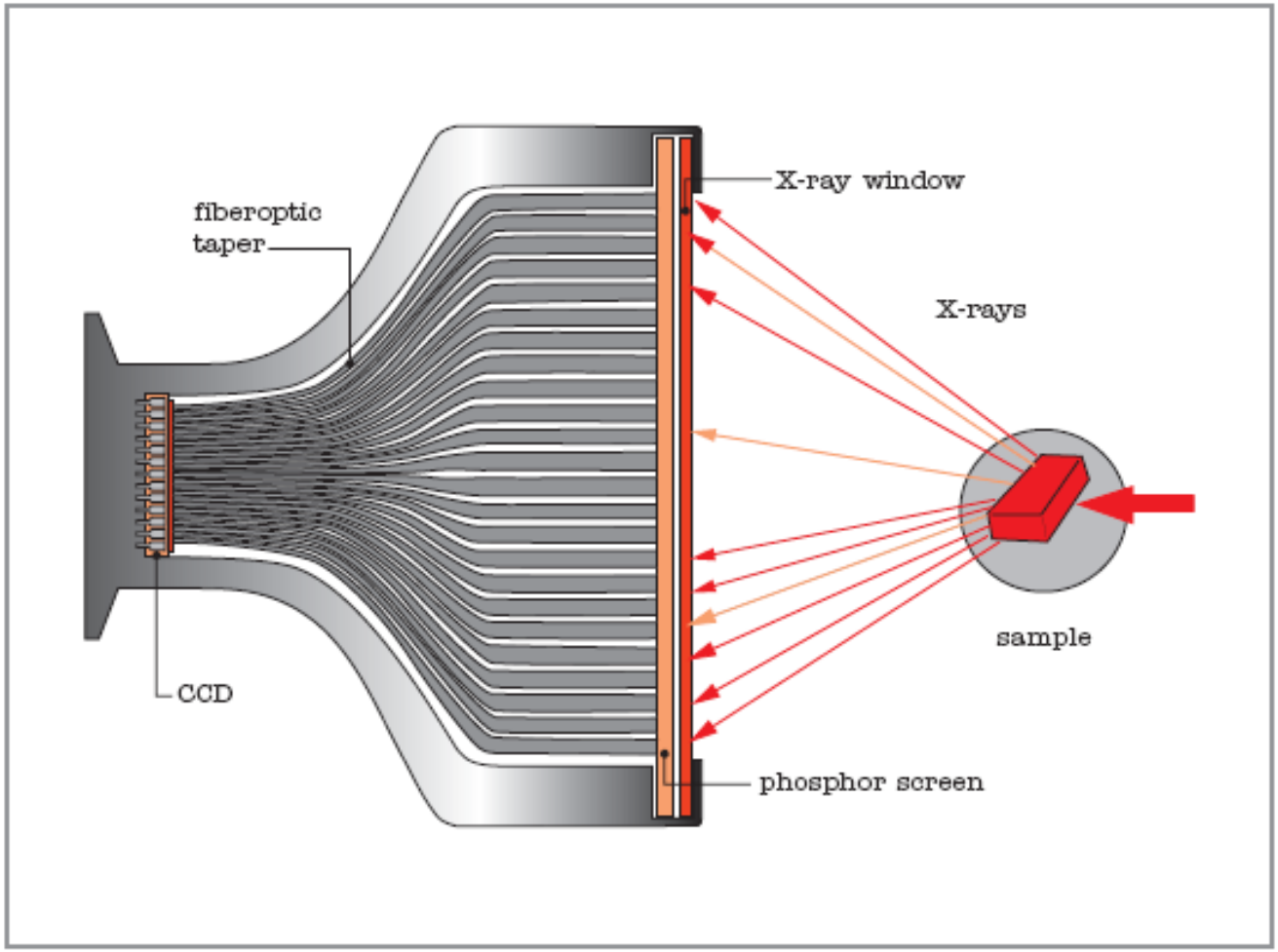


Figure 8. Diagram of a typical CCD detector used for X-ray diffraction.

Rentgenová difraktometrie monokrystal

The first atomic-resolution structure to be "solved" (i.e. determined) in 1914 was that of table salt. **The distribution of electrons** in the table-salt structure showed that crystals are not necessarily composed of covalently bonded molecules, and proved the existence of ionic compounds.
The structure of diamond was solved in the same year, proving the tetrahedral arrangement of its chemical bonds and showing that the length of C-C single bond was 1.52 Ångströms.
Other early structures included copper, calcium fluoride (*fluorite*), calcite ($CaCO_3$) and pyrite (FeS_2) in 1914; spinel ($MgAl_2O_4$) in 1915; the rutile and anatase forms of titanium dioxide in 1916; pyrochroite $Mn(OH)_2$ and brucite $Mg(OH)_2$ in 1919; and wurtzite (hexagonal ZnS) in 1920.

Historická data

* 1930 - první proteinový krystal (hemoglobin).
* 1934 - naměřeny první difrakční záznamy proteinu.
* 1953 - struktura DNA v podobě dvojité šroubovice (Watson & Crick).
* 1959 - struktury proteinu myoglobinu (Kendrew) a hemoglobin (Perutz).
* 1964 - metodika řešení struktur - přímé metody (Karle & Hauptman)
* Nobel Prices
  Röntgen 1901; Laue 1914; W. Bragg 1915; Watson & Crick 1962; Kendrew & Perutz 1962; Karle & Hauptman 1986 ; Deisenhofer Huber & Michel 1988.

Rentgenová difraktometrie monokrystal

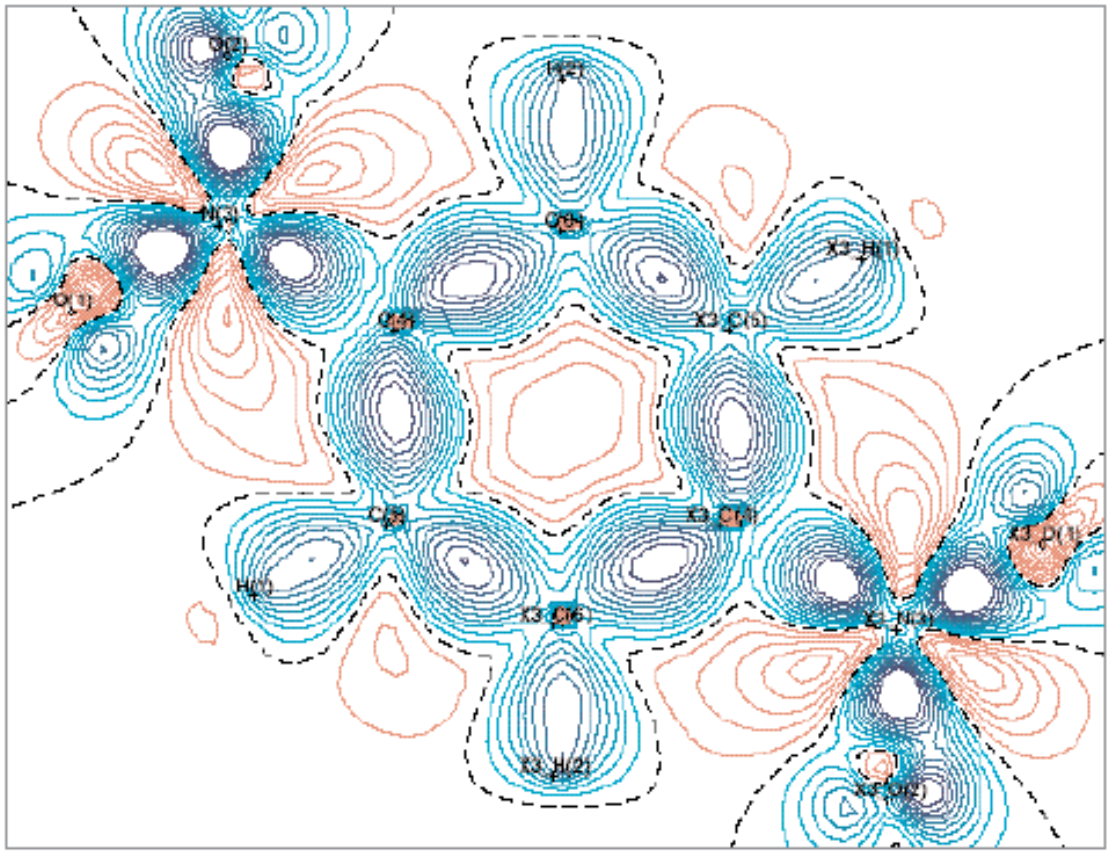
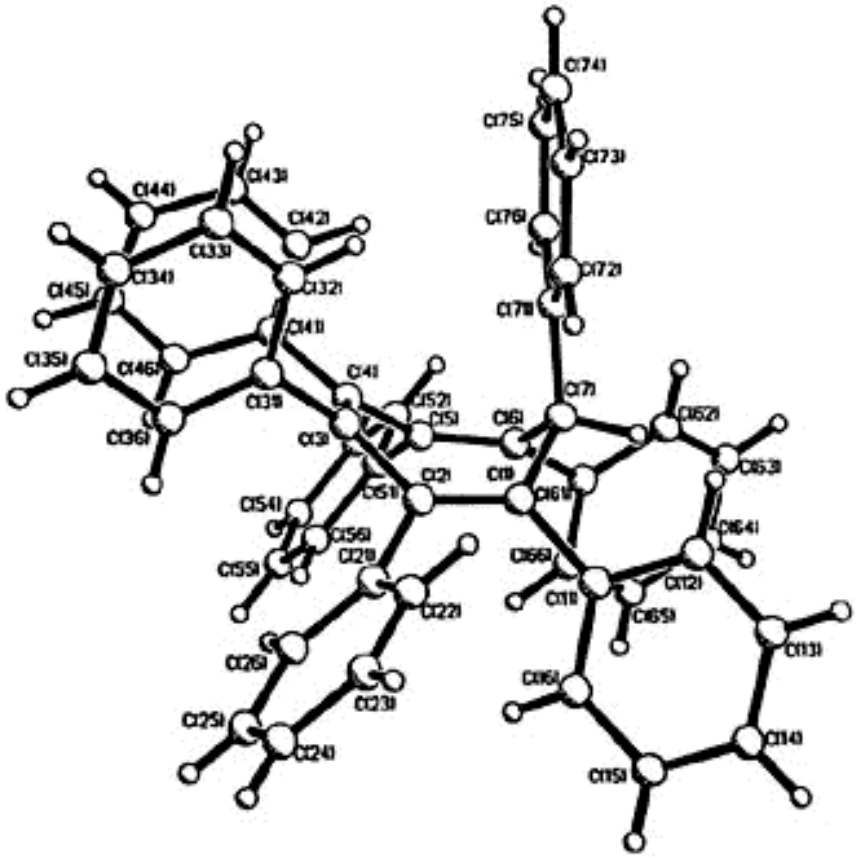
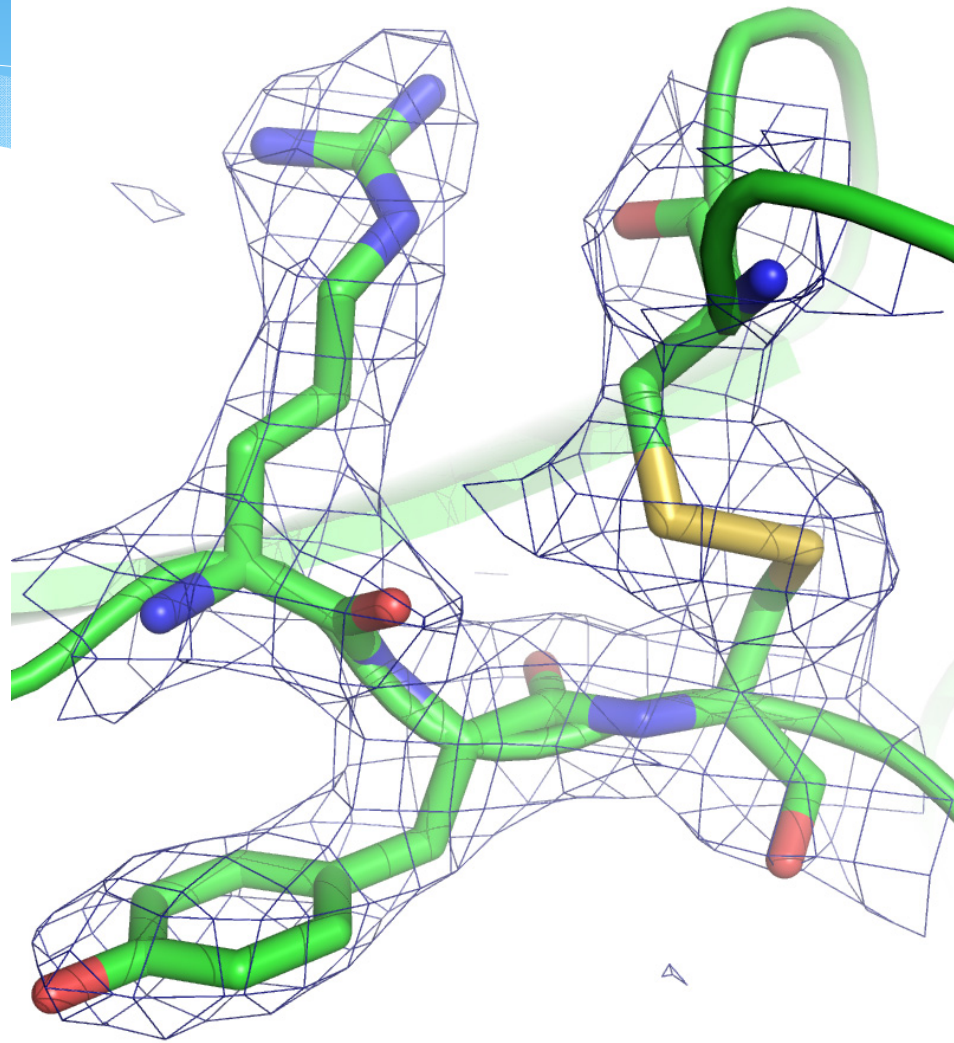


Figure 1. Electron density difference map for p-dinitrobenzene obtained by subtracting the pro-molecule electron density from the total electron density.

Rentgenová difraktometrie monokrystal





Rentgenová difraktometrie monokrystal

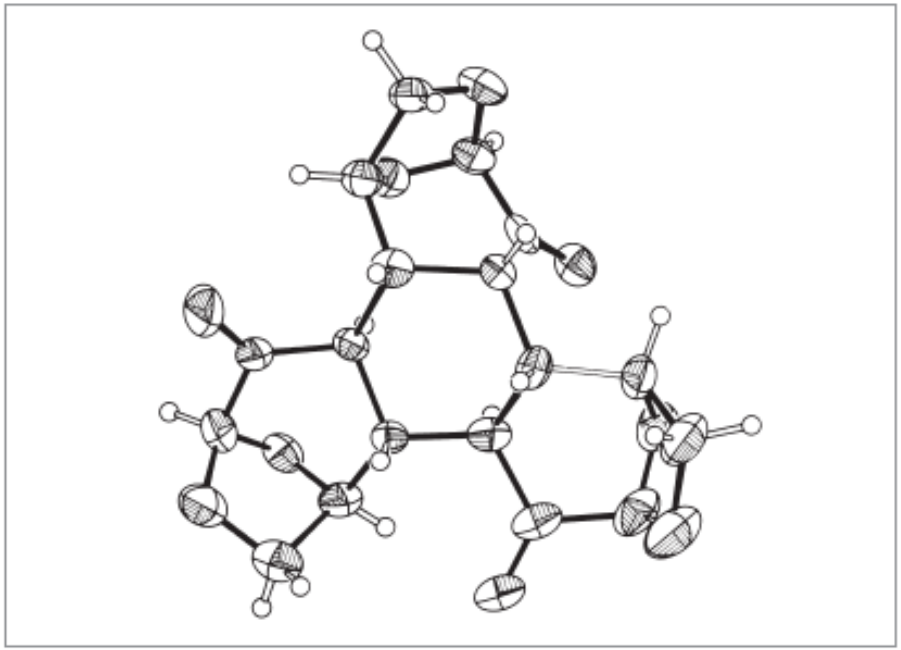


Figure 9. Thermal ellipsoid plot of the final structure of an organic compound ($C_{18}H_{18}O_9$).

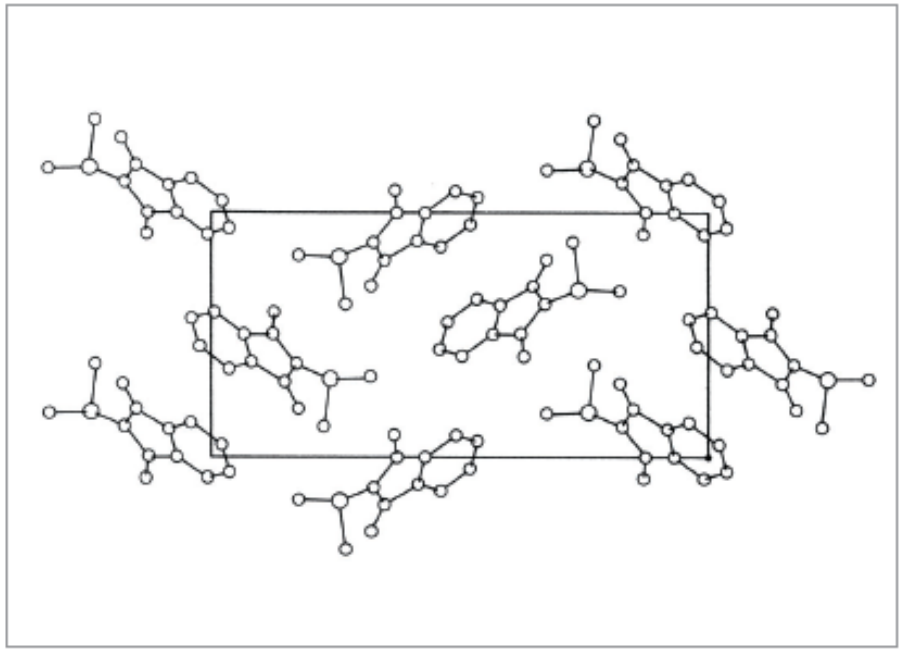
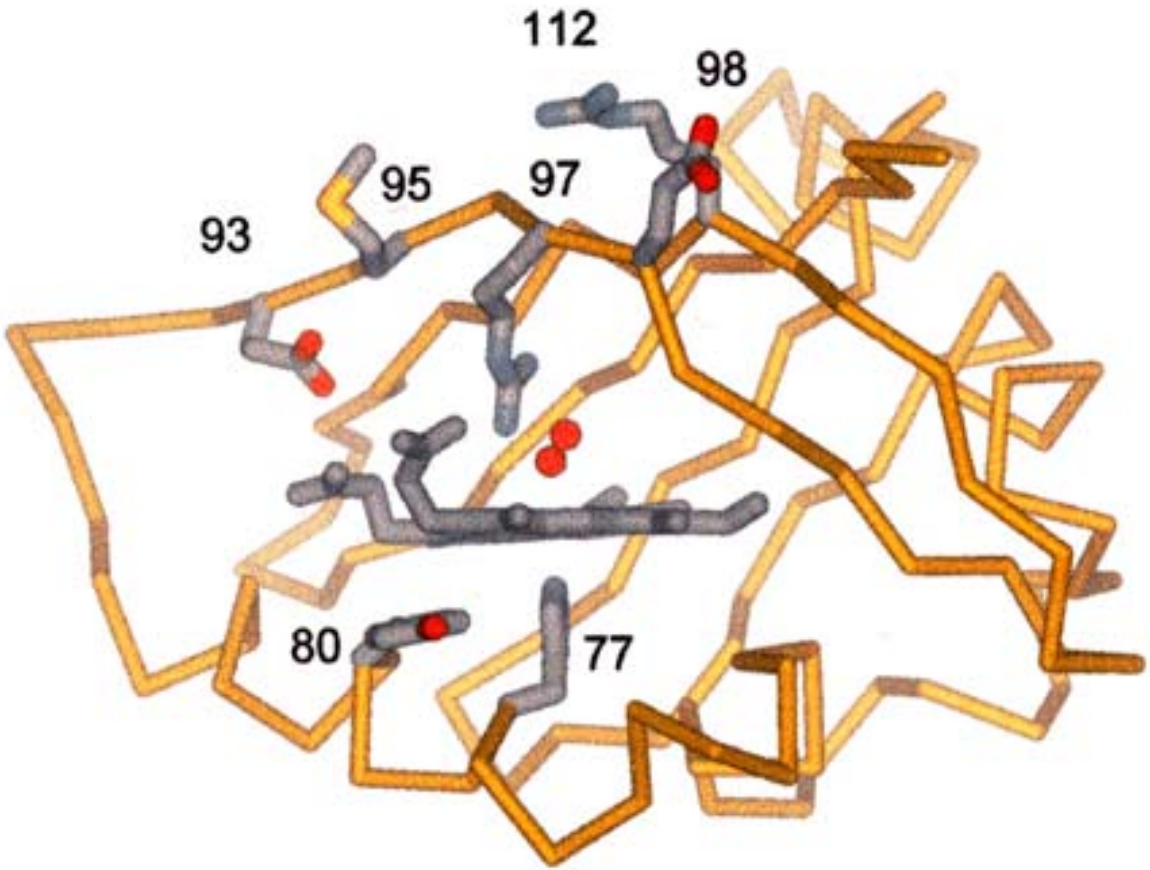


Figure 10. Unit-cell diagram showing the arrangement of molecules within the celll.

Rentgenová difraktometrie monokrystal

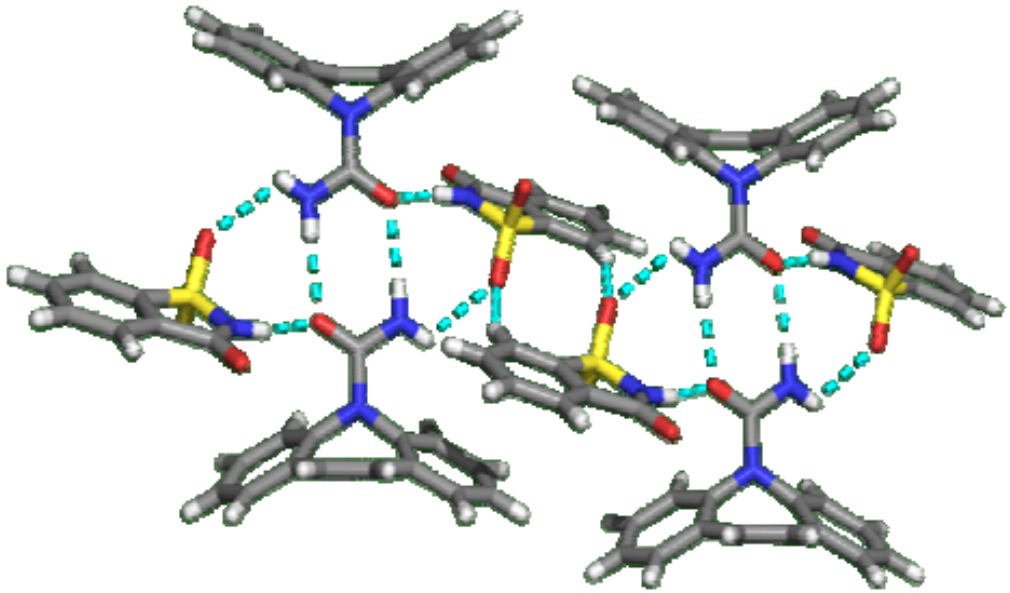


Mikrostrukturní rentgenografie

* kvalitativní a kvantitativní fázová analýza (0.1-100%),
* stanovení struktur krystalických fází(molekuly od 10-10000 atomů),
* určování velikosti krystalitů polykrystalických nanomateriálů(5-1000 Å),
* stanovování hustoty dislokací
* identifikaci textur (přednostní orientace krystalitů),
* měření vložených i zbytkových napětí,
* sledování rekrystalizačních jevů,
* studium fázových transformací
* studium mechanismu plastické deformace,
* určování orientace monokrystalů, výzkum jejich kvality,

Rentgenografie pro léčiva

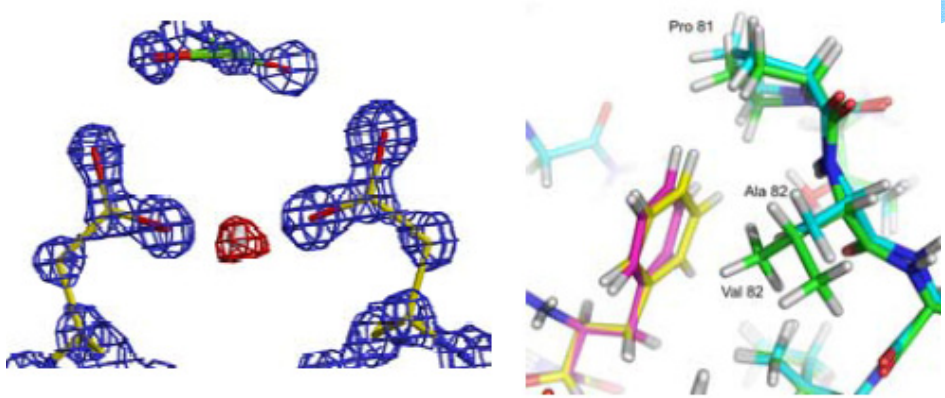
* Řešení struktury molekulárních kokrystalů – karbamazepin plus sacharin



Obr. 5. **Molekulární kokrystal karbamazepin : sacharin (1:1), jehož struktura byla vyřešena z RTG práškových dat** (obrázek laskavě poskytl prof. M. Zaworotko, University of South Florida)

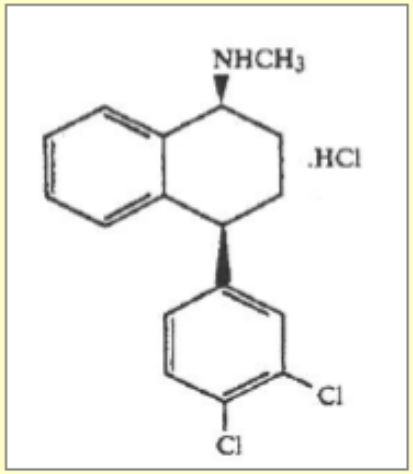
Rentgenografie pro léčiva

* vývoj inhibitorů retrovirové proteasy HIV (PDB molekuly měsíce června roku 2000) – rozlišení na úrovni 1,03 Angstromu

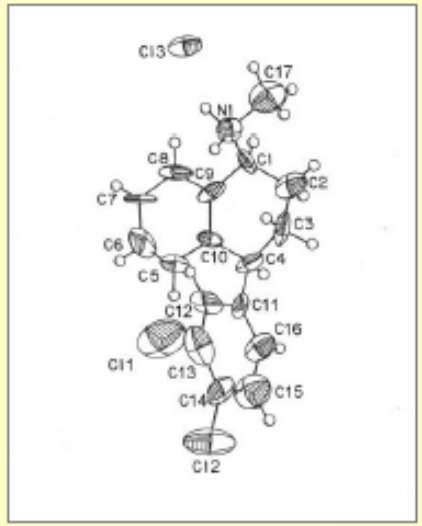


Obr. 11. **Detaily struktury komplexu HIV proteasy s fenylnorstatinovým inhibitorem, rozlišení 1,03 Å[39].** Detail vlevo: Katalytické místo; červeně konturovaná mapa diferenční elektronové hustoty uprostřed přísluší vodíkovému atomu; červeně vyznačené kyslíkové atomy karboxylových skupin proteasy a hydroxylové a karbonylové skupiny inhibitoru jsou kruhově propojeny vodíkovými vazbami. Detail napravo: Část inhibitoru v „podmístě P1" vazebné dutiny proteasy; při vazbě inhibitoru (vybarven fialově) k normální 82Val protease (zeleně) je úhel napojení boční fenylové skupiny k hlavnímu řetězci inhibitoru deformovaný, ale při vazbě ke mutované 82Ala protease je normální (žlutě a tyrkysově)

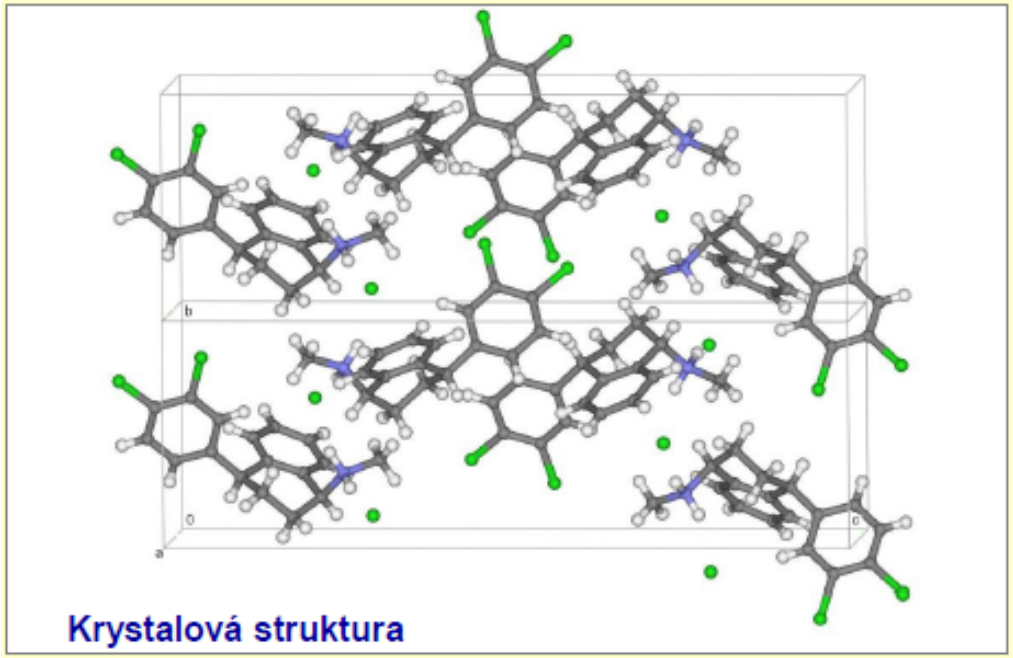
Rentgenografie pro léčiva



Chemická struktura



Molekulová struktura



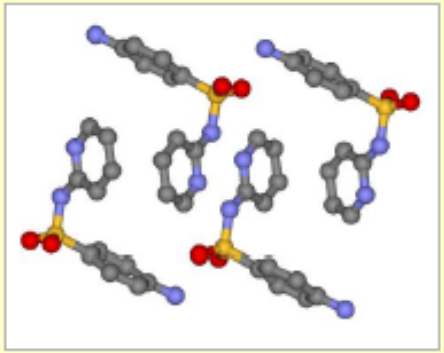
Krystalová struktura

Základní krystalografické parametry

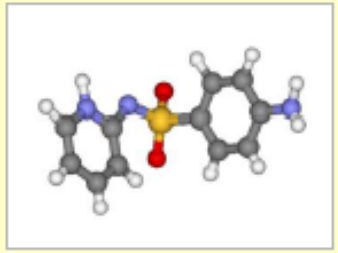
Cell dimensions (Å)	*a* = 8.004(5) *b* = 8.372(5) *c* = 25.21(2)
Cell volume (Å3)	*V* = 1689.3(6)
Space group	*P* 2 2 2 1 1 1
Crystal system	Orthorombic
Molecules/unit cell,	*Z* = 4
Density calculated (g/cm3)	ρ = *1.354*

Polymorfismus a polymorfy ve farmacii

Polymorfismus je schopnost API, ale i excipientů, tvořit různé pevné fáze (polymorfy), které se liší krystal.strukturou. Mezi polymorfy jedné entity existují polymorfní přechody. Polymorfy jedné entity se liší svými vlastnostmi (rozpouštěcí rychlostí, stabilitou, sorpcí vlhkosti, technolog. parametry atd.)

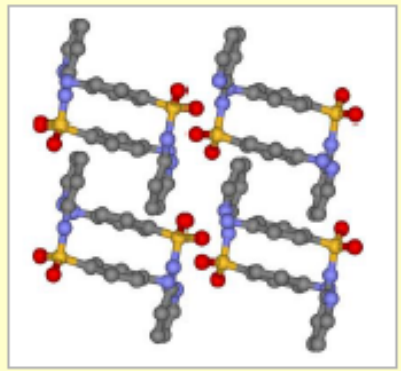


polymorf I

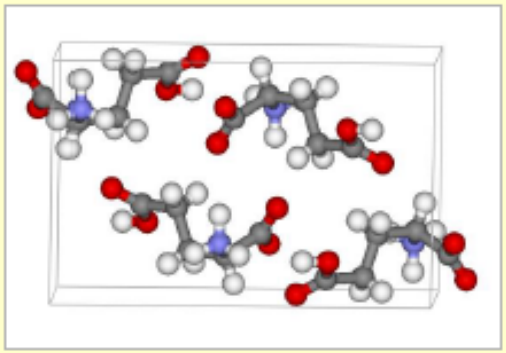


sulfapyridin

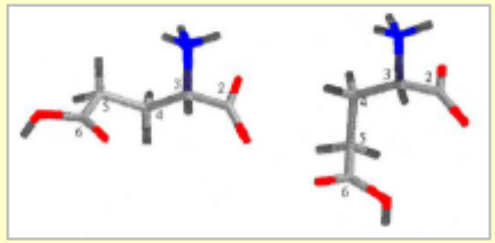
pakovací polymorfismus



polymorf II

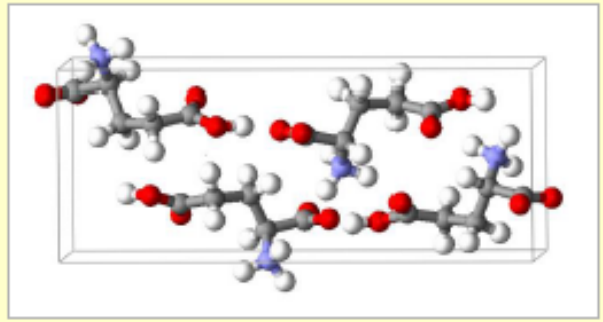


polymorf β



L – glutamová kyselina

konformační polymorfismus



polymorf α